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Crohn's Disease

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Abstract: **Crohn's disease is a chronic (long-term) inflammatory disease of the bowel (intestines). It primarily affects the small and large bowel, but can occur anywhere in the digestive tract. The inflammation causes uncomfortable and bothersome symptoms and may result in serious damage to the digestive tract. Abdominal pain, diarrhoea and weight loss are the most obvious symptoms. Making a definitive diagnosis is difficult, possibly requiring many different tests performed over a long period of time.**
Crohn's disease is one of the two major types of inflammatory bowel disease (IBD), The main difference between the two conditions is that, whereas Crohn's disease can affect any part of the digestive tract, ulcerative colitis affects only the large bowel and the rectum.
The number of people with Crohn's disease in New Zealand is not known but it has been estimated that nearly 17 in every 100,000 people in Canterbury have the disease, which is one of the highest reported rates in the world. Regional population differences may partially explain the high rate, as Crohn's disease is more common in Caucasian people than in Maori or Pacific Island people.

Keywords: **Crohn's disease in New Zealand, intestines.**

1. INTRODUCTION

Definition:

Crohn's disease is a chronic relapsing inflammatory bowel disease (IBD). It is characterized by a transmural granulomatous inflammation which can affect any part of the gastrointestinal tract, most commonly the ileum, colon or both. Unlike ulcerative colitis, there may be unaffected bowel between areas of active disease (skip lesions). The clinical course is characterized by exacerbations and remission.

Crohn's disease has several extra-intestinal manifestations, including iritis, arthritis, erythema nodosum and pyoderma gangrenosum.

Prevalence rate:

• The incidence and prevalence of Crohn's disease is increasing worldwide, with a systematic review reporting the highest incidence in Australia (29.3 per 100,000 population), Canada (20.2 per 100,000 population) and northern Europe (10.6 per 100,000).

• The prevalence in the UK is about 145 per 100.000 population

• Crohn's disease is more likely in those with a strong family history (first-degree relatives).

• Crohn's disease affects both sexes equally and is associated with excess mortality compared with the general population, with a standardized mortality ratio of 1.38.

• The onset of Crohn's disease has two age peaks: the first and largest peak occurs between the ages of 15-30 years; the second smaller peak is between 50-70 years. People over the age of 60 contribute to 10-15% of IBD diagnoses, compared to 5-25% made in children or adolescents

• However, Crohn's disease is also rapidly increasingly in children. The vast majority of affected children will need immunosuppressant treatment and around 20% will need treatment with biological agents.

Risk factors:

• There is a genetic element (15-20% will have an affected family member with IBD; 70% concordance in identical twins).

• Smoking increases risk three- to four-fold and smokers tend to have more aggressive disease and an earlier postoperative relapse.

• Other exacerbating factors include intercurrent infections (e g, upper respiratory tract infection (URTI) or enteric infection) and non-steroidal anti-inflammatory drugs (NSAIDs).

Possible causes of the disease:-

The precise cause of Crohn's disease is unknown. There are, however, several established risk factors, including the following:

• Family history (genetics)

• Smoking

• Use of oral contraceptives

• Ethnicity

• Environment

Interaction between the predisposing genetic factors (making a person more inclined to develop the condition), environmental factors, host factors (e g: a person's immune system function), and a triggering event (e g: bacterial infection) may be responsible for the development of the disease.

Although diet may affect the symptoms in patients with Crohn's disease, it is unlikely that diet is responsible for the disease.
There is a clear genetic predisposition for Crohn's disease. People with a relative who has the condition have 10-times higher likelihood of developing the disease than that of the general population. People are 30-times more likely to develop the condition if the relative with Crohn's disease is a brother or sister. It is also more common among relatives of people with ulcerative colitis.

Environmental factors, especially cigarette smoking, are also clearly involved in this disease. Tobacco smoking doubles the risk of both initial and recurrent Crohn's disease.

Improved food storage and reduced food contamination may also contribute to the development of Crohn's disease. This is the so-called 'hygiene hypothesis'. It proposes that the reduction in abdominal infections in developed countries has resulted in altered immune responses in the digestive tract. Bacterial infections that otherwise might only cause short-term disease instead may trigger a massive inflammatory response in the digestive tracts of susceptible individuals.

Diagnosis:

Crohn's disease is suspected in people who have experienced symptoms of abdominal pain, diarrhoea, and weight loss over a period of weeks or months. There is no single test that can establish the diagnosis of Crohn's disease with certainty, and Crohn's disease often mimics other conditions. For these reasons, it may take time and several investigations to arrive at a definite diagnosis of Crohn's disease.

Proper clinical separation from ulcerative colitis is important because the two conditions are treated differently. Ulcerative colitis causes inflammation only in the lower digestive tract (large bowel, rectum, or both), while Crohn's disease may cause inflammation anywhere in the digestive tract, including the mouth and anus. Another difference is that, in Crohn's disease, inflamed segments of the intestine may be separated by healthy segments, giving the condition characteristic 'skip lesions'.

The first part of the diagnosis involves the doctor taking a full medical and family history. A thorough physical examination is also conducted. Blood tests may be ordered to look for a low blood count (anemia) that may result from rectal bleeding, to measure the severity of inflammation, and to detect vitamin or mineral deficiencies. A bowel motion specimen may be needed to exclude infection as the cause of the symptoms being experienced.

Most people require part of their intestine to be examined, either by direct or indirect inspection. Direct inspection is carried out by endoscopy - a procedure in which a small flexible tube (endoscope) with a fibre-optic camera at its tip is inserted through the anus (colonoscopy or sigmoidoscopy) or mouth (gastroscopy). The doctor is able to see the lining of the rectum and colon on a television screen and can look for signs of inflammation that may indicate Crohn's disease. Small samples (biopsies) of the lining of digestive tract can be taken for analysis. Endoscopic visualization and biopsy are essential in the diagnosis of Crohn's disease.

Indirect inspection involves the use of computerized tomography (CT) scan, which is a type of computerized X-ray, and barium X-ray studies, in which a chalky substance (barium) is swallowed or administered into the rectum and colon and X-rays taken. The barium, which can be seen on the X-rays, improves the contrast of the X-ray images.

2. IBS SUB CLASSIFICATION ACCORDING TO THE ROME 111 CRITERIA

Irritable bowel syndrome (IBS) is a functional gastrointestinal disease with a high population prevalence. The disorder can be debilitating in some patients, whereas others may have mild or moderate symptoms. The most important single risk factors are female sex, younger age and preceding gastrointestinal infections.

Clinical symptoms of IBS include abdominal pain or discomfort, stool irregularities and bloating, as well as other somatic, visceral and psychiatric comorbidities. Currently, the diagnosis of IBS is based on symptoms and the exclusion of other organic diseases, and therapy includes drug treatment of the predominant symptoms, nutrition and psychotherapy.

Although the underlying pathogenesis is far from understood, aetiological factors include increased epithelial hyperpermeability , dysbiosis , inflammation, visceral hypersensitivity, epigenetics and genetics, and altered brain–gut interactions. IBS considerably affects quality of life and imposes a profound burden on patients, physicians and the health-care system.

IBS definition and subtypes: Rome III criteria:

Diagnostic criteria for irritable bowel syndrome (IBS) include recurrent abdominal pain or discomfort‡ at least 3 days per month in the past 3 months associated with two or more of the following:

• Improvement with defaecation

• Onset associated with a change in the frequency of stool

• Onset associated with a change in the form (appearance) of stool

Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis.

Discomfort means an uncomfortable sensation not described as pain. In pathophysiological research and clinical trials, a pain or discomfort frequency of at least 2 days per week during screening evaluation for subject eligibility.

IBS is a multifactorial disease. Hence, the underlying pathogenesis is considered complex and the precise molecular pathophysiology is far from understood. Several functional alterations have been described, such as altered visceral sensitivity, functional brain alterations, bowel motility and secretory dysfunctions, and somatic and psychiatric comorbidities.
Furthermore, gastrointestinal abnormalities — such as immune activation, gut dysbiosis (microbial imbalance), impaired mucosal functions, nerve sensitization, post-infectious plasticity, altered expression and release of mucosal and immune mediators, and altered gene expression profiles — have been associated with IBS. However, a coherent link between particular pathologies and IBS symptoms is yet to be established.

Moreover, results from studies assessing the contribution of most of the proposed pathological factors are inconsistent and the particular aetiology is often not related to particular gut symptoms.

For example, some studies have found evidence for gut micro-inflammation in IBS, whereas others could not confirm this finding, despite similar gastrointestinal symptoms. Such discrepancies, which also apply to the other biomarker candidates (not only to inflammation), strongly suggest the existence of IBS subpopulations, which, despite the similarity in gut symptoms, can be defined and distinguished by their pathophysiology and in-depth assessments of clinical and molecular biomarker clusters.

The same heterogeneity is evident with respect to clinical diagnosis and management. Indeed, medical treatment, nutritional intervention and psychotherapy lack consistent and homogeneous efficacy, but can be effective in some subgroups.

Pathophysiology:

Certain characteristic features of the pathologyseen point toward Crohn's disease; it shows a transmural pattern of inflammation, meaning the inflammation may span the entire depth of theintestinal wall. Ulceration is an outcome seen in highly active disease. There is usually an abrupt transition between unaffected tissue and the ulcer—a characteristic sign known as skip lesions.

Under a microscope, biopsies of the affected colon may show mucosal inflammation, characterized by focal infiltration of neutrophils,a type of inflammatory cell, into the epithelium. This typically occurs in the area overlyinglymphoid aggregates. These neutrophils, along with cells , may infiltrate the crypts, leading to inflammation (crypititis) or abscess (crypt abscess). granulomas, aggregates of macrophage derivatives known as giant cells, are found in 50% of cases and are most specific for Crohn's disease.

The granulomas of Crohn's disease do not show "caseation", a cheese-like appearance on microscopic examination characteristic of granulomas associated with infections, such astuberculosis. Biopsies may also show chronic mucosal damage, as evidenced by blunting of the intestinal atypical branching of the crypts , and a change in the tissue type (metaplasia) .

One example of such metaplasia, Paneth cell metaplasia, involves development of Paneth cells (typically found in the small intestine and a key regulator of intestinal microbiota) in other parts of the gastrointestinal system.

Complication of IBS:-

• Bowel obstructions

• Anal fissures (small tears in the anus that cause itching, pain, or bleeding)

• Ulcers (open sores in the digestive tract)

• Fistulas (ulcers on the wall of the stomach or intestine that allow gut contents to leak into other parts of the body)

• Malnutrition (such as vitamin and mineral deficiencies)

• Colon cancer

• Eye pain, itchiness, or redness

• Mouth sores

• Joint swelling and pain

• Skin sores, bumps, or rashes

Lifestyle and home remedies:-

Sometimes you may feel helpless when facing Crohn's disease. But changes in your diet and lifestyle may help control your symptoms and lengthen the time between flare-ups.

Diet:-

There's no firm evidence that what you eat actually causes inflammatory bowel disease. But certain foods and beverages can aggravate your signs and symptoms, especially during a flare-up.

It can be helpful to keep a food diary to keep track of what you're eating, as well as how you feel. If you discover some foods are causing your symptoms to flare, you can try eliminating them.

Foods to avoid:

• Limit dairy products. Many people with inflammatory bowel disease find that problems such as diarrhea, abdominal pain and gas, improve by limiting or eliminating dairy products. You may be lactose intolerant — that is, your body can't digest the milk sugar (lactose) in dairy foods. Using an enzyme product such as Lactaid may help as well.

• Try low-fat foods. If you have Crohn's disease of the small intestine, you may not be able to digest or absorb fat normally. Instead, fat passes through your intestine, making your diarrhea worse. Try avoiding butter, margarine, cream sauces and fried foods.

• Limit fiber, if it's a problem food. If you have inflammatory bowel disease, high-fiber foods, such as fresh fruits and vegetables and whole grains, may make your symptoms worse. If raw fruits and vegetables bother you, try steaming, baking or stewing them.

In general, you may have more problems with foods in the cabbage family, such as broccoli and cauliflower, and nuts, seeds, corn and popcorn. You may be told to limit fiber or go on a low residue diet if you have a narrowing of your bowel (stricture).

• **Avoid other problem foods:** Spicy foods, alcohol, and caffeine may make your signs and symptoms worse.

Other dietary measures:

• Eat small meals. You may find you feel better eating five or six small meals a day rather than two or three larger ones.

• Drink plenty of liquids. Try to drink plenty of fluids daily. Water is best. Alcohol and beverages that contain caffeine stimulate your intestines and can make diarrhea worse, while carbonated drinks frequently produce gas.

• Consider multivitamins. Because Crohn's disease can interfere with your ability to absorb nutrients and because your diet may be limited, multivitamin and mineral supplements are often helpful. Check with your doctor before taking any vitamins or supplements.

• Talk to a dietitian. If you begin to lose weight or your diet has become very limited, talk to a registered dietitian.

Smoking:

Smoking increases your risk of developing Crohn's disease, and once you have it, smoking can make it worse. People with Crohn's disease who smoke are more likely to have relapses and need medications and repeat surgeries. Quitting smoking can improve the overall health of your digestive tract, as well as provide many other health benefits.

Stress:

Although stress doesn't cause Crohn's disease, it can make your signs and symptoms worse and may trigger flare-ups. The association of stress with Crohn's disease is controversial.

When you're stressed, your normal digestive process changes. Your stomach empties more slowly and secretes more acid. Stress can also speed or slow the passage of intestinal contents. It may also cause changes in intestinal tissue itself. Although it's not always possible to avoid stress, you can learn ways to help manage it. **Some of these include:**

• Exercise. Even mild exercise can help reduce stress, relieve depression and normalize bowel function. Talk to your doctor about an exercise plan that's right for you.

• Biofeedback. This stress-reduction technique may help you reduce muscle tension and slow your heart rate with the help of a feedback machine. The goal is to help you enter a relaxed state so that you can cope more easily with stress.

• Regular relaxation and breathing exercises. One way to cope with stress is to regularly relax and use techniques such as deep, slow breathing to calm down. You can take classes in yoga and meditation or use books, CDs or DVDs at home.

Sign and symptoms:

Most people with Crohn’s disease are diagnosed during late adolescence and early adulthood (15-30 years of age), with a second spike in numbers occurring between the ages of 60 and 70 years, mainly in women.

Symptoms depend on the location and severity of the inflammation. Unpredictable symptomatic flare-ups and remissions characterize the long-term course of the disease.

Typical symptoms in a person with Crohn’s disease are abdominal pain and tenderness. Other Crohn’s disease symptoms include :

• Rectal bleeding

• Fever

• Weight loss, and loss of appetite

• Nausea, vomiting

• Malnutrition, and vitamin deficiencies

• Tiredness, lethargy
• Bone loss (osteoporosis)
• Anxiety (associated with coping with the condition)
• Stunted growth in children (which may occur many years before digestive symptoms appear)

Additionally, the area around the anus may be affected by ulcers, abscesses, fissures (small ulcerated cracks) or fistulas (small abnormal holes in the wall of the intestines or rectum).

3. METHODOLOGY

Twenty-six adult patients (with mean age of 34 ± 11 years), diagnosed with CD, None of the participants in this study had any other significant past medical history such as hypertension, diabetes mellitus, or hyperlipidemia.

Serum samples were drawn from peripheral veins of patients and healthy subjects in the morning after a 12 h fast. Whole blood sampleswere collected in vacutainer tubes containing no anticoagulant.

These vials were shaken thoroughly and incubated in upright position at room temperature for 30–45 min to allow coagulation.

The clotted samples were then centrifuged for 15 min at 2500 rpm. Next, the sera were carefully aspirated and collected in fresh polypropylene tubes, up to three-quarter of tubes capacity.

Any turbid sample was centrifuged and aspirated again to separate insoluble particles.

4. CROHN'S DISEASE QUESTIONNAIRE

All questions contained in this questionnaire are strictly confidential and will become part of your medical record. Personal information

Male ( )

Female ( )

Name ( )

Height _____

Weight _____

HEALTH HISTORY

1. Please list date of first diagnosis _____
2. Date of last major attack (duration and course of steroid therapy):
3. Is your client on any medications?
   - Yes, please give details
   - No
4. Please check if your client has had :
   - Hospitalizations for this disorder (list dates)
   - Surgery for this disorder (list dates + type)
   - Colonoscopy (list dates of most recent)
5. Extent + severity of disease:
6. Any complications of disease (to include anal absorption) psychiatric issues?
7. Any limitations on functional capacity?
8. Has your client smoked cigarettes in the last 12 months?
   - Yes, please give details
   - No
9. Does your client have any other major health problems (ex: liver disease, skin and oral lesions, polyarthropathy, etc.)?
   - Yes, please give details
   - No

5. RESULTS AND DISCUSSION

The most important metabolites in serum were selected based on previous studies. [26–28] The studied metabolites are amino acids (alanine, glutamine, leucine/isoleucine, lysine and valine), organic acids (lactate and creatine), lipid, and glucose.

In order to classify CD and healthy subjects, the data set was divided into two parts, training and test sets. The training set was used to build a model and identify the most relevant metabolites.

In order to test the predictive ability of the classification model, test set was employed. Approximately, 30% of the patient and normal samples have been randomly selected as test set.

Consequently, the training and test sets were composed of 39 and 16 1H NMR spectra, respectively. In order to reduce the risk of over-fitting, the test set was not used to make the model. Samples of the training set were classified using RF in which 500 trees were grown. The OOB data were used to estimate the prediction accuracy of classification.

Two chemical shifts of 0.99 and 1.03 have considerable impact for discriminating patient and normal samples. 1H chemical shifts at 1.03 and 0.99 ppm are assigned to δCH3 (valine) and βCH3 (isoleucine), respectively. The distribution of the area under peak values for Valine and Isoleucine metabolites in normal and patientsamples.

A confusion matrix, including knowledge about the number of correct and incorrect predictions, was compared with the real outcomes by a classification model. Performance of a classification model is commonly evaluated using the data in this matrix.

Four main categories of medication are used to treat inflammation in Crohn's disease:

Anti-inflammatory agents:

Aminosalicylates, such as meclizine (Pentasa) and sulphasalazine (Salazopyrin), are usually prescribed for mild-to-moderate Crohn's disease and are used to prevent flare-ups; corticosteroids, including budesonide (Entocort) and hydrocortisone acetate (Colifoam), are usually prescribed in short courses for active moderate-to-severe Crohn's disease. These medications act by reducing inflammation.

The aminosalicylates and corticosteroids can be taken by mouth (orally) and into the rectum (as an enema or suppository).

Antibiotics:

Such as ciprofloxacin (Cipflox), are used in the treatment of mild-to-moderate disease. It is thought that antibiotics work by altering the bacterial population of the intestine. They may also have an effect on the immune system.

Immunomodulators:

Including methotrexate (Methoblastin) and azathioprine (Imuran) are sometimes used to treat moderate-to-severe Crohn's disease, disease that does not respond to corticosteroids, and to prevent flare-ups. These medications work by suppressing the immune system.

Disease-modifying agents :

Such as infliximab (Remicade) and adalimumab (Humira) are used in the treatment of active moderate-to-severe Crohn's disease that has not responded to other medications. These medications act by disrupting the inflammatory process. Their use is somewhat restricted because they are expensive.

A well-balanced and nutritious diet is essential for anyone with Crohn's disease to prevent malnutrition and maintain good health. A healthy diet is even more important for growing children and adolescents with Crohn's disease who may experience delayed growth or pubertal development without adequate nutrition.

Vitamin (e g: vitamin D) and mineral (e g: iron and calcium) supplements might be necessary in some people.

Fibre supplementation may be beneficial in some people with Crohn's disease – fibre helps the healing of inflamed regions of the digestive tract.

In a of study of Caucasian New Zealanders with Crohn's disease, foods most often considered to be beneficial for symptoms included white fish, salmon and tuna, gluten-free products, and boiled potatoes and sweet potatoes.

Foods most often considered to make symptoms worse included grapefruit, nuts, chilli or chilli sauce, cream, salami, high energy drinks and beer.

It was not possible to identify specific foods that should be avoided by all people with Crohn's disease.

6. CONCLUSION

Because there is no cure for Crohn's disease the primary goals of treatment are the following:

• To achieve the best possible control of the inflammation with the fewest adverse effects from medication

• To permit life to be lived as normally as possible

• In children, to promote growth with adequate nutrition

A combination of medications is often required. The choice of medications used depends on the location of the inflammation, the severity of symptoms, and whether the aim is to treat a flare-up or to prevent further flare-ups. The types of side effects experienced, which can vary for different people, may also be a factor in the choice of medication used.

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