Clinical Approach to Chronic Diarrhea

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Clinical Approach to Chronic Diarrhea

Introduction

• Definitions.
• Pathophysiology.
• Etiology.

Clinical approach

• History.
• Physical.
• Investigations.

Common Clinical Forms
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Definitions

- **Diarrhea**: 
  
  Increased fluidity (↓ consistency).
  
  ↑ frequency.
  
  ± Increased volume.

- **Chronic**: >14 days-30 days duration.
  
  • Arbitrary.
  
  • Duration of the acute episode.

*Diarrhea is a symptom not a disease.*
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Pathophysiology

- **Osmotic**: osmotically-active substance (CHO, Mg, P, PEG, lactose, sorbitol,...)

- **Secretory**: stimulation of enterocyte receptor by (B. toxin, B. acid, SCF.acid, hormone/ VIP-secreting tumors (neuroblastoma, G.neuroma, carcinoids).

- **Motility disorders**:
  - ↑ Motility → ↓ Transit time (irritable bowel syndrome, etc).
  - ↓ Motility → B. overgrowth (pseudoobstruction, malrotation, etc).

- **Exudative disorders**: Inflammation (infection, IBD, etc).

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Etiology

– The postenteritis syndrome:
  - Prolonged diarrhea.
  - Follows acute gastroenteritis.
  - After clearance of the infection.

– Chronic enteritis: E. coli, S. enteritidis, G. lamblia.
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malabsorption syndromes

- **Generalized malabsorption**:  
  - involves all nutrients (CHO, proteins, fat).  
  - Examples: celiac disease, cystic fibrosis.

- **Selective Malabsorption**:  
  - CHO malabsorption (lactose, sucrose, glu-galact).  
  - Bile acid malabsorption, intest. lymphangiectasia.  
  - Acrodermatitis enteropathica, abeta-lipoproteinemia.  
  - Congenital chloride diarrhea.
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Etiology

- Cow’s milk sensitivity (allergy, intolerance).
  - Colitis (allergic).
  - Gastroenteritis (allergic).
  - Generalized malabsorption.

- Chronic nonspecific diarrhea (toddlers, IBS).

- Inflammatory bowel disease (UC, CD, IC).

- V.I.P-secreting tumors.
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Miscellaneous etiologies

- Anatomic (structural): malrotation, short bowel...etc.
- Idiopathic microvillus atrophy.
- Eosinophilic gastroenteropathy.
- Autoimmune enteropathy.
- Immune deficiency (T - B cell).
- Malnutrition \(\Rightarrow\) diarrhea.
# Clinical Approach to Chronic Diarrhea

## Table 3. Causes of chronic diarrhea in Saudi Arabia.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>KUH* number</th>
<th>KFU* number</th>
<th>Total number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post infectious syndrome</td>
<td>10</td>
<td>14</td>
<td>24 (25)</td>
</tr>
<tr>
<td>Protracted infections</td>
<td>6</td>
<td>6</td>
<td>12 (12.5)</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>10</td>
<td>–</td>
<td>10 (10.4)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>2</td>
<td>7</td>
<td>9 (9.4)</td>
</tr>
<tr>
<td>Idiopathic intractable diarrhea</td>
<td>–</td>
<td>8</td>
<td>8 (8.3)</td>
</tr>
<tr>
<td>Congenital chloride diarrhea</td>
<td>5</td>
<td>2</td>
<td>7 (7.3)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1</td>
<td>5</td>
<td>6 (6.2)</td>
</tr>
<tr>
<td>Acrodermatitis enteropathica</td>
<td>3</td>
<td>2</td>
<td>5 (5.2)</td>
</tr>
<tr>
<td>Glucose galactose</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>3</td>
<td>1</td>
<td>4 (4.2)</td>
</tr>
<tr>
<td>Cow’s milk protein</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Intolerance</td>
<td>2</td>
<td>2</td>
<td>4 (4.2)</td>
</tr>
<tr>
<td>Intestinal lymphangiectasia</td>
<td>2</td>
<td>2</td>
<td>4 (4.2)</td>
</tr>
<tr>
<td>Immune deficiency</td>
<td>3</td>
<td>–</td>
<td>3 (3.1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47 (100%)</strong></td>
<td><strong>49 (100%)</strong></td>
<td><strong>96 (100%)</strong></td>
</tr>
</tbody>
</table>

*KKUH = King Khaled University Hospital, Riyadh (Central Province)*  
*KFHU = King Fahad Hospital of the University, Alkhobar (Eastern Province)*
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Clinical approach: the history

- Family history.
- Age at onset.
- Dietary history and appetite.
- Temporal relationship: food/diarrhea.
- Type of stool and associated symptoms.
- Growth and development.
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Clinical approach: the physical examination

• Growth parameters: weight, length, Wt for length (or BMD, HC).

• Nutritional status: signs of malnutrition, wasting.

• Special signs:
  – Abdominal distension (malabsorption).
  – Dermatitis (allergy, Acroderm. Enteropathica, vit. Def.).
  – Edema (P C malnutrition, protein-losing enteropathy).
  – Arthritis (inflammatory bowel disease).
  – Retinitis, ataxia (abetalipoproteinemia).
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Clinical approach: investigations

Routine (first line)

- Blood: CBC diff., ESR, electrolytes, BUN, creatinine TSP, albumin.
- Urine: microscopy, and culture.
- Stool:
  - Microscopy (cells, fat, parasites), and culture.
  - Occult blood.
  - pH and reducing substances.
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Clinical approach: investigations

Further (second line)

- **Blood**: Antiendomysial or anti tissue trans glutaminase A antibodies, triglycerides, cholesterol, lipoprotein electrophoresis, Ca, P, alk.phos. Enterocytes autoantibodies.

- **Stool**: 72H. stool fat, alpha-1-antitrypsine level.

- **Sweat chloride**, Barium meal with SBFT.

- **Endoscopy and biopsies (upper, lower) for histopathology**.

- **Elimination/challenge tests**.
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Differential Diagnosis of Villous Atrophy

- Celiac disease
- The Postenteritis syndrome
- Chronic enteritis (i.e. Giardiasis)
- Cow’s milk protein allergy
- Autoimmune enteropathy
- Congenital microvillous atrophy
- Eosinophilic gastroenteropathy
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Common Clinical Forms of chronic diarrhea

Chronic non specific diarrhea
The post enteritis syndrome
Gluten-sensitive enteropathy
Chronic nonspecific diarrhea.

Clinical profile

- The onset is gradual.
- The diarrhea is mild:
  - 3 - 6 BMs / day.
  - Contains undigested vegetables.
  - First BM (morning) may be firm and large.
- Normal growth: (FTT 2 to dietary restrictions).
- No evidence of gastrointestinal pathology.
**Chronic nonspecific diarrhea.**

**Management**

- Avoid exclusion diets.
- Avoid excessive fluid intake (fruit juice).
- Prescribe a normal diet for age with normal fat.
- Medication generally not helpful.
  - Role of ASA, Loperamide.

The postenteritis syndrome.

**Definition**
Diarrhea >2wks, following acute GE, associated with F.T.T and no evidence of other causes.

**Prevalence**
5-20%, commonest cause of ch.D in DC.

**Risk factors**
- Age: < 3 months.
- Nutrition: Lack of breastfeeding, malnutrition, nutrition during acute GE.
- Severity of the preceding gastroenteritis.

The postenteritis syndrome.

The etiology is multifactorial
- Intestinal villous injury.
- Secondary CHO intolerance, bacterial overgrowth.
- Relative pancreatic insufficiency.

The diagnosis is clinical.

The management is non specific
- Nutrition: provide sufficient calories as tolerated.
- Drugs: Limited indication (cholestyramine, ASA, peptobisthmol, loperamide, antibiotics).
Gluten-sensitive enteropathy (CD).

Pathogenesis

- Genetic predisposition:
  - Multiple cases in families.
  - High prevalence in first degree relatives (10%).
  - High concordance rate in monozygotic twins (75%).
  - Association with DQ alleles on DRw17, DR7, and DR5.
  - These H.L.A (chr.6) molecules:
    - are present in 95% of CD patients Vs 20-30% in NI subjects.
    - are involved in binding gliadin and their presentation to T cells.

- Environmental = exposure to gluten (gliadin fraction) - a protein in certain cereals (barelly, oats, wheat, rye...).
Gluten-sensitive enteropathy (CD)

Clinical aspects of celiac disease

The classical presentation: Gastrointestinal

Non-gastrointestinal

Conditions with ↑ prevalence of CD
Gluten-sensitive enteropathy (CD)

The classical presentation: Gastrointestinal

Chronic diarrhea
abdominal distension,
muscle wasting.
Anorexia,
irritability, apathy.
Non-gastrointestinal manifestations of CD

- Dermatitis herpetiformis
- Short stature
- Enamel hypoplasia
- Osteopenia, osteoporosis
- Unexplained anemia
- Delayed puberty
- ALT elevation
- Arthritis
- Intractable seizures
Gluten-sensitive enteropathy (CD)

Conditions with ↑ prevalence of CD

- Type 1 diabetes mellitus
- Autoimmune thyroiditis
- Down Syndrome
- Turner Syndrome
- Williams Syndrome
- Selective IgA deficiency
- First degree relatives of CD patients

*Recommended screening after 3 years of age*
Gluten-sensitive enteropathy (CD)

Laboratory findings

- Anemia, hypocalcemia, hypoalbuminemia.
- Antiendomysium/anti tissue transglutaminase A abs.
- Histopathology: villous atrophy, crypt hyperplasia, and inflammatory infiltrate.
Gluten-sensitive enteropathy (CD)

Sensitivity and specificity of CD serology

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGA-IgA</td>
<td>0.52-1.00</td>
<td>0.92-0.97</td>
</tr>
<tr>
<td>- IgG</td>
<td>0.52-1.00</td>
<td>0.50</td>
</tr>
<tr>
<td>EMA-IgA</td>
<td>0.88-1.00</td>
<td>0.91-1.00</td>
</tr>
<tr>
<td>TTG-IgA</td>
<td>0.92-1.00</td>
<td>0.91-1.00</td>
</tr>
</tbody>
</table>
Gluten-sensitive enteropathy (CD).

Diagnostic criteria:

- Measurement of IgA antibody to human recombinant tissue transglutaminase (TTG). The others are no longer recommended. (limitation = IgA deficiency).

- Small bowel biopsy is recommended in all cases for confirmation.

- The diagnosis is definitive only when there is complete response to GFD

Gluten-sensitive enteropathy (CD).

Management

Gluten-free diet (G.F.D)
Eliminate ALL sources of gluten in the diet.

Nonresponse to GFD
Noncompliance
Consider other diagnoses:
– sensitivity to other proteins or food.
– Immune deficiency (IgA).
– Intestinal lymphoma.
G.F.D for life (malignancy). ? Transient GI(5%).

THANK YOU FOR YOUR ATTENTION