Non-infectious causes of gastrointestinal disease in migrants

Stuart Bloom
University College London Hospitals
NHS Foundation Trust

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Case scenarios

- Bloody diarrhoea in 75 year old Bangladeshi
- Iron deficiency anaemia in 50 year old non-English speaking Asian woman
- Diarrhoea in 20 year old law student
- Abdominal pain and diarrhoea in 30 year old Polish decorator
- Managing urgent GI case in community
Bloody diarrhoea in 75 yo bangaladeshi man

- 75 yo from East End: type 2 diabetic
- Home to Bangladesh
- Returns with bloody diarrhoea; stool cultures negative
- Sigmoidoscopy shows confluent colitis to mid transverse colon
Size of the problem

- **Prevalence**
  - UC 250/100,000
  - CD 100/100,000

- **Incidence**
  - CD 5-10/100,000/yr
  - UC 10-15/100,000/year

- 80% lifetime operation rate for CD, 20% colectomy incidence for UC
- 10% receive Mabs costing c10k/year
- IBD confers Increased risk of colorectal cancer
- Total cost to UK economy 0.7-1 billion/year
Reasons to study IBD in Migrants

• Evolving pattern of disease in developing countries
• An evolving problem in some Migrant communities (South asians, Askenazi Jews)
• Studying migrant populations may give insights into environmental risk factors
IBD in migrants: issues

• IBD incidence/prevalence in developing world
• Incidence and prevalence in UK migrants
• IBD course in migrants
  – Extent of disease
  – Complications
  – Risk of relapse
• Colorectal cancer risk in migrants
Global map of UC incidence

Ng, Gut 2013
## Incidence of UC and CD in Asia

<table>
<thead>
<tr>
<th>Location (reference)</th>
<th>Year</th>
<th>Incidence (cases/10^5/year)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>Japan (9)</td>
<td>1991</td>
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<td>Japan (10)</td>
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<td>Seoul, Korea (11)</td>
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<td>1986–1988</td>
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<td>Hong Kong (12)</td>
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<td>Singapore (13)</td>
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<td>Kuwait (15)</td>
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<tr>
<td>Sultanate, Oman (16)</td>
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Yang IBD 2001
Annual incidence of UC and CD in Japan

Yang 2001 IBD
Incidence of UC and Crohn’s among Migrant Asians

<table>
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<tr>
<th>Location (reference)</th>
<th>Year</th>
<th>Incidence (cases/10^5/year)</th>
<th>Ulcerative colitis</th>
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Yang 2001 Inflamm Bowel diseases
Prevalence of UC and CD in migrant Asians

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<thead>
<tr>
<th>Location (reference)</th>
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<th>Crohn’s disease</th>
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<td>Leicestershire, England (28)</td>
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<td>Upper Galilee, Israel (27)</td>
<td>1986</td>
<td>19.3</td>
<td>64.2</td>
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<tr>
<td>Jews</td>
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<td></td>
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<tr>
<td>Southern Israel (29)</td>
<td>1992</td>
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<tr>
<td>Jews</td>
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<td>50.6</td>
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</tbody>
</table>

Yang IBD 2001
IBD course in migrant populations

- In developing countries, UC incidence rises first, then CD
- No difference in disease extent: 30% proctitis, 30% left sided, 30% pancolitis
- Higher incidence of UC in male Asians may reflect reluctance of females to seek care
- No major differences in local or systemic complications between Asian migrants and Europeans
- Some evidence of lower colectomy rates in South Asian migrants in Leicester
Environmental risk factors

- Smoking: no good geographical data. Smoking likely does not cause CD but modulates it once present.
- Appendicectomy: associated with lower incidence of UC.
- Dietary factors: saturated fat intake in Japanese.
- Microbiota:
  - new techniques are stimulating much research: hygiene and cold chain hypotheses.
  - Gastroenteritis can predispose to IBD.
- Sun exposure and vitamin D levels.
- Modest link between oral contraceptives and IBD.
Iron deficiency in migrants

- Globally 2 billion people are anaemic
- Iron deficiency most widespread nutritional disorder in the world
75yo south indian

- Presents with UTI, found to be anaemic
- Hb 9.3, MCV 69, CRP 45, Ferritin 35, Iron 8 (7-26), TIBC 75 (41-77) IBS 10.5%

- Is this Iron deficiency?
- According to what criteria?
Diagnosing Iron deficiency

• Ferritin is accurate measure of Iron stores but is acute phase protein made in liver
  – Normal value is over 13 but only when CRP is normal
  – If CRP is raised, lower limit of Ferritin is 100
• TIBC reflects Transferrin – acute phase protein made in liver
• Key measure is Iron Binding saturation: should be over 15%
Differential of microcytic deficiency in Migrants

- Iron deficiency
  - Dietary deficiency
  - Malabsorption due to GI problems or diet high in phytates (legumes, whole grains) or phenols (tannins in tea, wine)
- Blood loss (mennorhagia, infestation with hookworm, schistosomiasis, ascariasis)
- Increased iron needs in growth and pregnancy
- Thalassaemia
- Lead poisoning: eye kohl, calabash chalk
Diarrhoea in a 20 year old law student

- BO 5x/day
- Up at night
- Weight loss 7 lb
- New job
- Pressure at home

- Is this more suggestive of IBD or IBS?
- Do you need to refer to secondary care?
- Are there any tests which can help you decide?
Faecal Calprotectin

Faecal Calprotectin testing in Primary Care
Following a survey of all GP practices, GPs felt the benefits of FCP testing to be

- Provides additional reassurance for patients who may have anxiety or uncertainty about IBS or IBD
- Reduced number of referrals from those tests which have been clearly negative. During this project, a total of 129 patients were spared from referral to secondary care
- Identified cases for referral that may not previously have been clinically indicated
- Greater confidence in diagnosing IBS within primary care without the need for endoscopy.

“Whilst not a formal research trial, NTAC feels that this work is highly suggestive that FCP is a useful tool in the diagnosis of IBS within primary care. “

Northumberland Primary Care IBS Pathway (Based on NICE CG61 Pathway)

**Irritable Bowel Syndrome likely if:**
Abdominal pain or discomfort which is
- Relieved by defaecation, or
- Associated with altered bowel frequency or stool form,
And at least two of the following:
- Altered stool passage (straining, urgency, incomplete evacuation)
- Abdominal bloating (more common in women than men), distension, tension or hardness
- Symptoms made worse by eating
- Leathery, nausea, backache and bladder symptoms may support diagnosis

**Investigations:**
- Faecal Calprotectin (FCP) – request on ICE and send stool sample to lab
- NB: Stop NSAIDs 4 weeks prior to FCP testing
- Bloods: FBC, ESR, CRP, TTG (to exclude other diagnoses)
- Consider CA125 in women

**FCP negative**

**FCP indeterminate**

**FCP positive**

**FCP strongly positive**

**1. Abdominal pain, bloating, change in bowel habit >6 months, and**
2. **Age <60 years**

**“Red Flag” symptoms:**
- Unintentional weight loss
- Rectal bleeding
- Family history of bowel/ovarian cancer
- Anaemia
- Abdominal/rectal mass

**No red flag symptoms**

Consider referral to consultant – 2 week rule referral if cancer suspected

**Probable IBS. Low probability of organic pathology.**
Lifestyle advice and dietary advice sheet. Physical activity.
Consider:
- Dietetic referral
- Antispasmodic medication (mebeverine, peppermint oil)

**Repeat test after 4 weeks. If negative manage as above for IBS. If still indeterminate or positive and symptoms persist then refer to consultant**

**Moderate probability of organic pathology. Referral to consultant.**

**High probability of organic pathology. Fast-track referral to consultant using referral form. Patient will be seen within 2 weeks.**

**Referral to consultant**
Abdominal pain and diarrhoea in 30 yo polish decorator

- Epigastric discomfort radiating to back
- Little relief from antacids/PPI
- Loose stools
- Weight loss 5 kg

- 3 relevant investigations?
- Likely diagnosis?
- Management?
Faecal elastase as a marker of pancreatic insufficiency

Table II. [FE-1] compared to clinical diagnosis: all cases.

<table>
<thead>
<tr>
<th>[FE-1]</th>
<th>Clinical diagnosis positive</th>
<th>Clinical diagnosis negative</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200 μg/g</td>
<td>32</td>
<td>9</td>
<td>41</td>
</tr>
<tr>
<td>&gt;200 μg/g</td>
<td>9</td>
<td>55</td>
<td>64</td>
</tr>
<tr>
<td>Totals</td>
<td>41</td>
<td>64</td>
<td>105</td>
</tr>
</tbody>
</table>

Sensitivity = 78%, specificity = 76.6%, positive predictive value (PPV) = 78%, negative predictive value (NPV) = 85.9%, diagnostic accuracy = 82.9%.
Faecal elastase as a marker of pancreatic insufficiency

### Faecal elastase-1 screening for chronic pancreatitis

Table III. [FE-1] compared to clinical diagnosis: mild acute pancreatitis (Ranson score <3).

<table>
<thead>
<tr>
<th>[FE-1]</th>
<th>Clinical diagnosis positive</th>
<th>Clinical diagnosis negative</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200 µg/g</td>
<td>31</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td>&gt;200 µg/g</td>
<td>8</td>
<td>49</td>
<td>57</td>
</tr>
<tr>
<td>Totals</td>
<td>39</td>
<td>50</td>
<td>89</td>
</tr>
</tbody>
</table>

Sensitivity = 79.5%, specificity = 98%, positive predictive value (PPV) = 96.9%, negative predictive value (NPV) = 86%, diagnostic accuracy = 89.9%.
Helicobacter pylori

- Effectiveness of HP eradication has fallen largely due to clarithromycin resistance
Helicobacter pylori treatment in the era of increasing antibiotic resistance

David Y Graham, Lori Fischbach

“The time is long overdue to let clinicians know that currently used treatments for HP are not adequately effective, and alternative therapies with over 95% treatment success need to be identified”

Gut 2010; 59:1143-53
Recommendations for treating HP

- Do not use ‘legacy triple therapy’ consisting of a PPI, clarithromycin and amoxicillin unless it has been proven to be highly effective locally (eg, eradication >90% in per-protocol analyses)
- Use higher doses of drugs (eg, 500 mg of clarithromycin, metronidazole and tetracycline) unless it has been shown that lower doses are equally effective
- Use 14 day duration unless a shorter duration has been shown locally to be equally effective (eg, for clarithromycin and fluoroquinolones)
- Do not use a triple regimen containing clarithromycin, if clarithromycin is commonly prescribed locally or the patient has taken clarithromycin in the past, for any indication
- Avoid fluoroquinolones if a quinolone (eg, ciprofloxacin, levofloxacin or moxifloxacin) has been given previously, even for any indication
- Following treatment failure, do not reuse drugs for which resistance is likely to have developed (ie, clarithromycin and fluoroquinolones)
Recommendations for treating HP

- Use a treatment which achieves >90% eradication in local population
- If this is not known, use e.g.
  - 14 day quadruple regimen (PPI, amox, clari, nitroimidazole)
  - 10 days sequential treatment (PPI plus amox 5 days, followed by PPI, clari, nitroimidazole for 5 days)
  - Bismuth based quadruple regimens can be used as first line therapies
  - Newer drugs furazolidine, nitazoxanide need evaluating