Review Article

# Infectious intestinal disease: do we know it all?

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## Abstract

Infectious intestinal disease (IID), with associated high morbidity and considerable mortality worldwide, causes a wide spectrum of illness. This ranges from mild discomfort to illness with severe complications. The economic burden from direct and indirect costs may be high. It is acquired by oral ingestion of micro-organisms which are transmitted from person to person; via food or water or through contact with animals or contaminated objects. Viruses are the commonest cause in developed countries. In Malta, medical practitioners and laboratories are the main source of data on IID. However, under-reporting is a problem. In order to fill in the lacunae in information on the disease burden, population-based-studies are required. Along with other countries, Malta has embarked on a number of studies to describe and quantify under-reporting of IID. This may assist in strengthening the surveillance system which, in combination with other measures, should result in an improvement of the control of IID.

## Key words

Infectious intestinal disease, surveillance, under-reporting

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## Introduction

The term **infectious intestinal disease** (IID) is used to describe gastrointestinal symptoms (diarrhoea, vomiting and abdominal pain) due to micro-organisms or their toxins. It is one of the leading causes of morbidity and mortality worldwide.[1-3] In less developed countries, the mortality rate from this category of disease is slowly decreasing but the incidence remains very high.[4-5] In more developed countries, improvements in hygiene and treatment of disease have radically reduced the number of deaths while the clinical course is often self-limiting. However, the morbidity remains high.[6]

IID causes a wide spectrum of diseases ranging from minor discomfort to extreme dehydration which may result in death. Most episodes are self limiting. However, some may lead to complications. It has been estimated that 2-3% of IID cases develop a variety of secondary long term illnesses.[7] The most recognised of these are irritable bowel syndrome,[8-9] Guillain-Barré syndrome,[10-11] reactive arthritis and haemolytic uraemic syndrome.[12-13]

The economic burden of IID to society is high.[14-16] There are direct costs involved which include those relating to general practitioner (GP) consultations, laboratory tests, hospital admissions and medications. Indirect costs include losses in income and productivity.[17]

## Aetiology of infectious intestinal illness

IID is acquired predominantly by oral ingestion of micro organisms or their toxins. They are transmitted by close contact with other infected persons; by the consumption of contaminated food or water; through contact with animals or by contact with contaminated objects (fomites).[18] Some pathogens are associated with a specified mode of transmission such as the rotavirus which is mainly non-foodborne. However, most pathogens have multiple modes of transmission (Table 1).

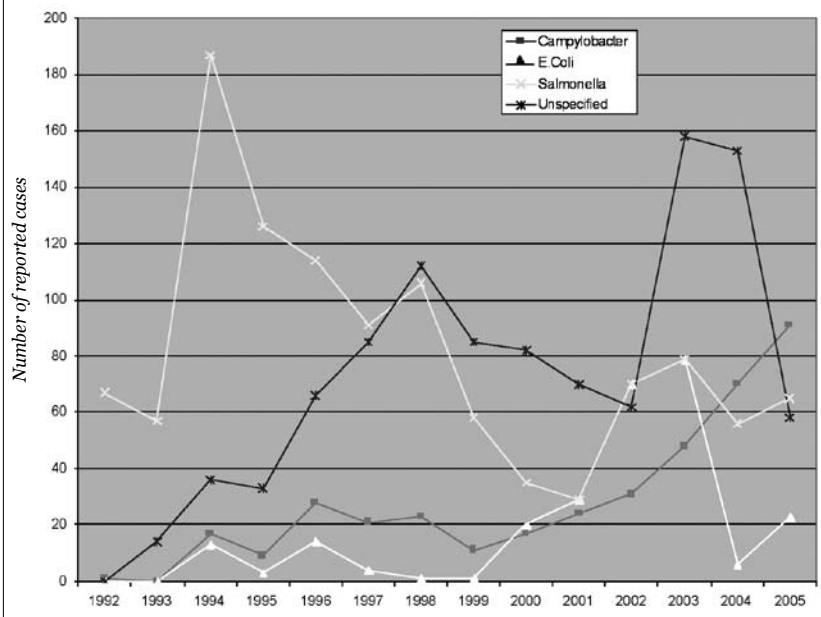
Viral infections are the commonest cause of IID in the community. Noroviruses are suspected to be the most common cause in the United States.[19] Other viruses include rotavirus,[20] sapovirus, adenovirus and astrovirus. The commonest bacterial agents responsible for IID are *Campylobacter* and *Salmonella*. Other bacteria include *Escherichia coli*, *Shigella*, *Staphylococcus aureus*, *Bacillus cereus* and *Yersinia*. The main protozoa causing infectious intestinal disease are *Cryptosporidium* and *Giardia lamblia*.[21]

In Malta, *Salmonella* was the commonest identifiable

***Table 1**: Micro-organisms known to cause IID, their source and symptoms*

| ***Micro-organism*** | ***Common sources*** | ***Symptoms of infection*** |
|---|---|---|
| *Campylobacter* | Eating contaminated meat (especially undercooked poultry); drinking contaminated water or unpasteurised milk | Often bloody, sometimes watery diarrhoea lasting 1 day to a week or more |
| *Salmonella* | Eating contaminated food, contact with reptiles (iguanas, snakes, turtles) | High fever, abdominal cramps, nausea, vomiting, diarrhoea that may or may not be bloody. Symptoms usually last 3 to 7 days |
| *Shigella* | Person-to-person contact, especially in day-care centres | May be mild or severe. In mild cases, watery, loose stools. In severe cases, high fever, severe abdominal cramps, painful passage of stool containing blood and mucus. Symptoms usually last about a week without treatment |
| *Escherichia coli* O157:H7 | Eating undercooked ground beef or drinking unpasteurised milk or juice; swimming in contaminated pools; person-to-person contact; touching infected animals and then putting | Sudden abdominal cramps, watery diarrhoea that usually becomes bloody within 24 hours, haemolytic-ureamic syndrome fingers in one's mouth |
| *Entamoeba histolytica* | Eating or drinking contaminated food or water | Bloody diarrhoea, abdominal pain, weight loss lasting 1 to 3 weeks. Can cause infection in liver and other organs |
| *Enterotoxigenic E. coli* | Eating or drinking contaminated food or water | Frequent watery diarrhoea. Usually lasts 3 to 5 days |
| *Vibrio cholerae* | Eating or drinking contaminated food or water | Painless, watery diarrhoea; vomiting. Can lead to massive fluid loss, shock. |
| Other types of *Vibrio* | Shellfish | Watery, diarrhoea, often with little nausea or vomiting |
| *Staphylococcus aureus* | Eating food contaminated by toxins produced by bacteria | Severe nausea and vomiting beginning about 2 to 8 hours after eating contaminated food |
| *Clostridium perfringens* | Eating food contaminated by toxins produced by bacteria | Usually mild. When severe, abdominal pain, abdominal expansion, severe diarrhoea, dehydration, shock. Symptoms usually begin 8 to 16 hours after eating contaminated food |
| Viral infections *(rotaviruses, norovirus, astroviruses, enteric adenoviruses)* | Epidemic and often seasonal | Frequent watery diarrhoea; vomiting and fever (milder in astroviruses). Usually lasts 2 to 7 days (10 days or more for enteric adenoviruses) |
| *Giardia* | Drinking contaminated stream water; person-to-person contact, particularly in day-care centres | Diarrhoea, nausea, loss of appetite. More long-term illness (lasting several days to several weeks) may occur, with grassy stools, abdominal bloating, gas, and weight loss |
| *Crytosporidium* | Drinking contaminated water; person-to-person contact. People with AIDS are particularly susceptible | Watery diarrhoea, crampy abdominal pain, nausea, vomiting |

***Figure 1**: Reported sporadic foodborne illness in Malta 1992-2005 by aetiological agent*



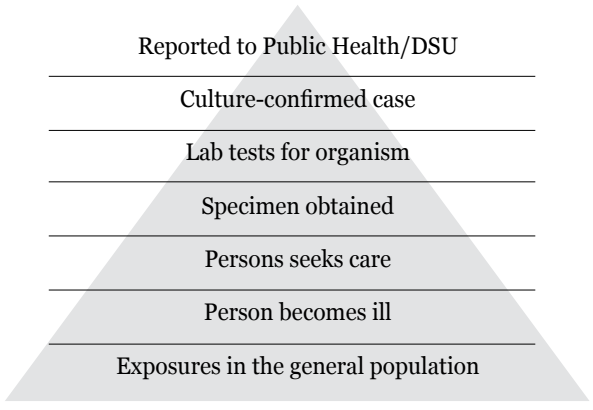

pathogen in cases of IID over recent years up to 2003. However, as of 2004 the number of reported cases of *Campylobacter* is higher than that for *Salmonella*.[22] A substantial number of notified cases in the same year are still defined as unspecified where the aetiological agent has not been identified (Figure 1).[23] In these cases, the pathogen may not identified. Alternatively it may well be a pathogen not yet identified. These will become apparent with time and investigation.

It may well be that the majority of the cases labelled as unspecified in Malta are of viral origin, since tests for viruses are not routinely used and particularly the laboratory test for norovirus is not available locally to date.

## Sources of information on infectious intestinal illness in Malta

In Malta, a small island state with traditionally strict infectious disease legislation, surveillance of infectious diseases dates back over a century. During the 19th century, the importance of improving the sanitary condition of the Island was highlighted through a number of legal ordinances introduced in 1875. The Sanitary Office was set up through these laws and was responsible for, amongst other public health issues, the investigation and control against infective diseases and for the keeping of statistics.[24] Today, the Disease Surveillance Unit, within the Public Health Department, is responsible for the surveillance of infectious intestinal disease. This unit receives notifications from general practitioners, hospital physicians and laboratories. The majority of notifications received include cases, which required hospitalisation or referral for stool culture analysis. Notifications from general practitioners are very few even though these have a statutory obligation to notify. To be included in the present surveillance system, an individual must first present to the health care provider who should notify the case. Of those that present to the health care provider, only a small proportion of specimens are submitted for microbiological testing. Naturally, only the severe cases would require hospitalisation. Hence, the surveillance system captures only a tiny fraction of the infectious intestinal disease that is actually occurring in the community. This indicates that there must be significant lacunae in information describing the magnitude of infectious intestinal disease, especially at the population level. Figure 2 represents the relatively unknown quantity of IID and an undefined portion that is reported.

***Figure 2**: The reporting fraction of IID in Malta*



## The international situation

The problem of under-reporting is a recognised problem internationally.[25-30] In order to better estimate the burden associated with IID, research is required to provide information to base estimates. A number of international initiatives have been designed to determine the burden of disease.

***WHO Global Salm-Surv.*** This an international capacity-building programme which strengthens national laboratory-based surveillance and outbreak detection of diseases commonly transmitted via food.[31]

***WHO Sentinel Sites Project***. This project defined surveillance systems in four categories based on the ability of the system to generate information on foodborne illness.[32] Category 1 included countries where no formal surveillance existed; Category 2 included countries with syndromic surveillance; Category 3 included countries with laboratory-based surveillance and Category 4 included those with integrated food-chain surveillance. The countries with Category 3 and 4 surveillance systems were recommended for burden studies. Jordan was chosen as the first sentinel site for this project.

***International Collaboration on enteric diseases: the Burden of Illness Studies.*** This was set up to bring epidemiologists conducting population studies together to share information and collaborate on international studies.[33] This network includes researchers from more than 30 countries amongst which are the United States, Canada, Australia, Ireland, Scotland, the United Kingdom, Japan, the Netherlands and Malta who are performing studies in an attempt to estimate the actual burden from IID. The main aims of this network are to:

- Foster communication between researchers via a list-server, conference calls, and an annual face-to face-meeting.
- Create a forum for sharing information about the design, implementation and analysis of studies on the burden of illness.
- Provide advice to countries wishing to conduct burden of illness studies.
- Contribute to global estimates.

A number of countries have undertaken national initiatives in estimating the burden of infectious intestinal disease. The first countries to embark on community studies to estimate the burden of IID were England, The Netherlands and the United States.[25, 34-37] After this a number of other countries conducted similar studies. Some researchers used a prospective cohort study whilst others used a retrospective cross-sectional study.

***England.*** A prospective population cohort study was performed in England over the period 1993-1995.[25, 38-39] Cohorts from 70 general practices were recruited and stool samples were obtained and tested for bacteria, viruses and parasites. It was estimated that 19.4% (CI ± 2.7) of the population of England suffered from IID in a year and 3.3% of the population presented to their GP with IID. The most common aetiologic agents were norovirus, *Campylobacter* species, rotavirus, and non-typhoidal *Salmonella* species.

***The Netherlands.*** A similar study was carried out in the Netherlands during the period 1998-1999 where 60 practitioners reported the number of consultations for acute gastroenteritis that occurred each week. An age-stratified random sample of patients identified from the same registers was selected for a community-based cohort. This provided an estimate of 28.3% (CI ± 6.3) of the population suffered from gastroenteritis[36] and 1.4% consulted their GP.[35] This study also investigated a broad range of pathogens causing gastroenteritis.[9] The most common pathogen at community level was norovirus (11%).[21]

***United States***. The FoodNet population survey, established in 1996 out as part of CDC's Emerging Infectious Programme is based on retrospective self-reported symptoms.[37] During 1996-1997, this survey reported 11.0% (CI ± 0.8) of the people suffering from diarrhoeal illness in the 4 weeks before the interview.

***Ireland.*** A retrospective telephone study of self-reported symptoms of gastroenteritis that was performed during the period 2000 to 2001 in Ireland estimated that 4.5% (CI ± 0.8) of the population reported suffering from acute gastroenteritis in the 4 weeks prior to the interview with a rate of 0.60 episodes per person per year.[40-41]

***Australia.*** A retrospective study conducted in Queensland in 2001 via OzFoodNet, estimated that 13.6% (CI ± 2.4) of the adult cases (18 years or older) and 13.9% (CI ± 8.1) of children (7 months to 4 years) reported diarrhoea in the preceding month.[42]

***Canada.*** The National Studies on acute gastrointestinal Illness conducted a retrospective population based study which estimated a monthly prevalence of 10% and an adjusted incidence rate of 1.3 episodes per person per year.[43]

***Norway.*** A retrospective population-based study was carried out in 1999-2000 using a self-administered postal questionnaire. The prevalence of acute gastroenteritis was 14.4% (CI ± 2.6) of which 17% consulted a physician.[44]

## Situation in Malta

Information on the burden of IID illness is lacking in Malta. Various issues were considered in the choice of the methodology for a possible exploratory study.[45] A cohort study is not applicable in a country like Malta where no general practitioner based patient lists exist, with patients referring to any doctor they wish and hence, a doctor would not be able to follow up patients prospectively. Hence, a cross sectional study was chosen as the method to estimate the prevalence of IID in Malta. The advantages of the cross-sectional methodology include the fact that it is less expensive and can be performed more quickly, enabling a larger sample size, hence, decreasing Type II error*. Attrition of participants is not a concern and there is no difficulty and cost in maintaining contact with the

* Type II error: the error of rejecting a true null hypothesis i.e. declaring that a difference exists when it does not.

**Table 2:** *Food poisoning - sporadic cases which inlcude non-resident cases and imported cases*

| *Year* | *1992* | *1993* | *1994* | *1995* | *1996* | *1997* | *1998* | *1999* | *2000* | *2001* | *2002* | *2003* | *2004* | *2005* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Campylobacter* | 1 | 0 | 17 | 9 | 28 | 21 | 23 | 11 | 17 | 24 | 31 | 48 | 70 | 91.0 |
| *E. Coli* | 0 | 0 | 13 | 3 | 14 | 4 | 1 | 1 | 20 | 29 | 70 | 79 | 6 | 23.0 |
| *Salmonella* | 67 | 57 | 187 | 126 | 114 | 91 | 106 | 58 | 35 | 29 | 70 | 79 | 56 | 64.7 |
| *Unspecified* | 0 | 14 | 36 | 33 | 66 | 85 | 112 | 85 | 82 | 70 | 62 | 158 | 153 | 58.0 |
| **Total** | **68** | **71** | **253** | **171** | **222** | **201** | **242** | **155** | **154** | **152** | **233** | **364** | **285** | **236.7** |

subjects since they are not followed up. Another factor is that this type of study can capture community cases, since it does not rely on persons presenting to their GP. There are a number of disadvantages to this approach which includes difficulty in separating the chronology of cause and effect because of the short time studied and the inherent biases (selection, confounding and information bias).

Four studies have been launched in Malta in order to estimate the incidence of infectious intestinal disease at various levels and to identify where and how cases are lost along the surveillance chain. These include:

1. ***A Community based survey*** interviewing an age-stratified random sample of the population to estimate the baseline incidence of self-reported infectious intestinal disease in the community and to estimate the proportion of cases which do not present to the health care system and are notified, thereby quantifying under-reporting of infectious intestinal disease.
2. ***A Sentinel Surveillance study*** consisting of intensified surveillance by a number of GPs for a defined period of time in order to estimate the true number of cases presenting to GPs with IID and to test the feasibility of carrying out sentinel surveillance in Malta.
3. ***A Knowledge, Attitude and Practice survey of physicians*** consisting of a focus study and a postal survey of a sample of local physicians to assess their attitudes and awareness of the notification system in order to identify the reasons behind under-notification or delayed notification, with a view to developing recommendations aimed at reducing this problem.
4. ***A Laboratory Study*** consisting of interviews at local laboratories to identify practices in laboratories that impact on the sensitivity of finding an aetiologic agent in submitted stool specimens and their attitudes towards notification.

## Conclusion

In a small island state such as Malta, the epidemiology of infectious disease ought to be more practical and complete. Describing and quantifying under-reporting may assist in strengthening the surveillance system of IID by:

a) identifying where and how cases are lost along the surveillance chain
b) finding ways to reduce loss of data and
c) developing correction factors to compensate for a known magnitude of under reporting.

Strengthening the national surveillance system in combination with other measures should result in a marked improvement in the ability to detect, investigate and control food and water-borne enteric pathogens.

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