

# ORIGINAL ARTICLES

## Clinical Management of Children with Suspected or Confirmed *E. coli* O157 Infection

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### Abstract

Scotland continues to report higher rates of infection with *Escherichia coli* O157 than elsewhere in the UK. Infection with *E. coli* O157 usually manifests as acute, afebrile, painful, bloody diarrhoea and is the commonest cause of Haemolytic Uraemic Syndrome (HUS), an important cause of childhood renal failure. In 1996 an outbreak of *E. coli* O157 infection in Central Scotland, resulted in over 500 cases and 17 deaths. Ten years on, high-profile outbreaks of *E. coli* O157 infection in Scotland still result in cases of HUS and fatalities. We sought to identify outcomes and describe pre-hospital clinical management strategies using prospective, national surveillance of paediatric HUS cases, from 2003 to 2006 inclusive. We recommend that children who present with acute, afebrile, and painful bloody diarrhoea be referred to hospital as early as possible for appropriate clinical management.

### Introduction

Acute bloody diarrhoea is a medical emergency. It is very likely to be due to infectious colitis and is often associated with considerable abdominal discomfort. Infection with *E. coli* O157 typically causes diarrhoea, which in 90% of cases becomes bloody after 1-3 days and bloody diarrhoea often prompts patients or their families to seek medical attention from their GP. Approximately 15% of children with *E. coli* O157 infection develop Haemolytic Uraemic Syndrome (HUS) <sup>1</sup> and in most cases, renal function recovers although long-term renal and/or extra-renal sequelae such as hypertension and renal insufficiency can develop. <sup>2</sup> Several clues help differentiate *E. coli* O157

infections from colitis caused by other bacteria. Most cases of *E. coli* O157 infection are afebrile on presentation <sup>3</sup> and abdominal pain (especially on defaecation) and abdominal tenderness is usually more severe than in other forms of bacterial gastroenteritis. <sup>4</sup>

Previous surveillance of childhood HUS in Scotland identified *E. coli* O157 in over 90% of cases. <sup>5</sup> Clinical surveillance is particularly relevant in Scotland, where consistently higher rates of infection with *E. coli* O157 have been reported than in other parts of the UK or Europe. (Figure 1) Here, we present results from a population-based epidemiological surveillance study of HUS, with particular emphasis on this syndrome and clinical management of children with suspected or confirmed *E. coli* O157 infection.

### Methodology

Cases of paediatric HUS (age <16 years) were ascertained prospectively over four years of an active, continuing national surveillance programme in 2003. Consultants from 6 hospitals throughout Scotland were approached for participation in the study. Consultants in paediatrics, nephrology, haematology and microbiology were sent fortnightly e-mails and asked to indicate whether they had a 'case of HUS to report' or 'nil return'. Further information on cases was obtained by telephone including date of onset, gender, age, hospital and possible public health implications (for example infection with *E. coli* O157). A unique study number was created to maintain subject anonymity. Questionnaires, information sheets and consent forms were subsequently sent to the reporting clinician via post or e-mail. All completed forms and

questionnaires were returned to Health Protection Scotland (HPS) and the data were entered into an EpiInfo (Version 6) database.

The statistical significances of associations between categorical variables were investigated using chi-squared or Fisher's Exact tests. Normally distributed quantitative variables were compared using t-tests with results displayed as mean (+/- standard error of the mean). All analyses were performed using SPSS (version 11) with a significance level of 5%.

## Results

Between 1 January 2003 and 31 December 2006 inclusive, 81 reports of paediatric HUS were provided to HPS. In this survey, paediatric HUS was primarily associated with *E. coli* O157 infection and this association was highly significant (74 cases of 81,  $p < 0.001$ ). Other infectious causes of HUS included *E. coli* of non-O157 serotype (serotypes O177, O145 and O-unidentifiable, one patient each). Two cases of HUS associated with pneumococcus were also reported.

We explored the pre-hospital clinical management of HUS cases with suspected or confirmed *E. coli* O157 infection and found that treatment of these cases with non-steroidal anti-inflammatory drugs (NSAIDs) was significantly associated with development of renal impairment ( $p < 0.001$ ). Furthermore, pre-hospital treatment of HUS cases (with suspected or confirmed *E. coli* O157 infection) with antibiotics was significantly associated with neurological impairment ( $p < 0.007$ ) and dialysis dependence ( $p < 0.03$ ).

## Discussion

Failure to appreciate the potential severity of *E. coli* O157 infection and the possible development of HUS may result in avoidable morbidity and even death. The trend in platelet count is the most useful predictor of the development of HUS.<sup>1</sup> We strongly recommend that children who are suspected or known to have *E. coli* O157 infection be referred to hospital for assessment. Another reason for referral

is that patients with *E. coli* O157 colitis are highly infectious, and infection control is often difficult to practice in the community.<sup>1</sup> A third reason is that intravenous volume expansion with saline appears to confer nephroprotection.<sup>6</sup>

Anuric renal failure associated with HUS necessitates dialysis, lengthens hospitalisation and is more likely to result in chronic sequelae.<sup>6</sup> Children with *E. coli* O157 infection who present early, have a greater risk of developing HUS,<sup>3</sup> possibly because they have more fulminant and severe vascular injury. Children who present to general practitioners (GPs) early therefore present a paradox; although they are more likely to develop HUS, they also stand to benefit most from an early opportunity to receive parenteral volume expansion before renal insufficiency ensues during an interval when such therapy is presumably safe.<sup>6</sup>

Guidance for the diagnosis and management of suspected or proven *E. coli* O157 infection was prepared by the Scottish Infection Standards and Strategy Group<sup>7</sup> in 2003. The authors recognise that bloody diarrhoea may not only be the result of infection with *E. coli* O157 but may be a symptom of a condition, which is non-infectious. Although intussusception and ischaemic colitis should be considered in the appropriate age and setting, these conditions can be confused with or mask enteric infections and the threshold for hospital referral should be low, as GPs rarely have the opportunity to recognise patients at such an appreciable and predictable risk of shortly developing anuric renal failure, as when children present early with *E. coli* O157 infection.

In line with the SISS guidelines, GPs should refer patients to hospital, when the risk of *E. coli* O157 infection is high, or its consequences are likely to be severe. This includes any occurrence of bloody diarrhoea in infants and children below the age of ten years, abdominal pain or protracted diarrhoea as well as those requiring parenteral rehydration. Furthermore, antibiotics should not be administered to patients with suspected or definite Verocytotoxin producing *Escherichia coli* (VTEC) infections, as there is no evidence to suggest that this improves

the clinical course of infection.<sup>8</sup> In a prospective study, children infected with VTEC who were treated with antibiotics had a higher rate of HUS<sup>3</sup> and a study of the Central Scotland *E. coli* O157 outbreak also revealed that antibiotics might also increase the risk of HUS developing in adults.<sup>9</sup> Nevertheless, results from our study reveal that children with suspected or confirmed *E. coli* O157 infections are still prescribed antibiotics and this is associated with neurological impairment and dialysis dependence.

In conclusion, we recommend that children with suspected or confirmed *E. coli* O157 infection be referred to hospital as early as possible for appropriate clinical management. Such patients are highly infectious to others, infection control is often difficult to practice in the community<sup>1</sup> and intravenous volume expansion with saline appears to confer nephroprotection.<sup>6</sup> Furthermore, antimotility agents, non-steroidal anti-inflammatory drugs, and opioid narcotics should also be avoided.<sup>1</sup>

#### References

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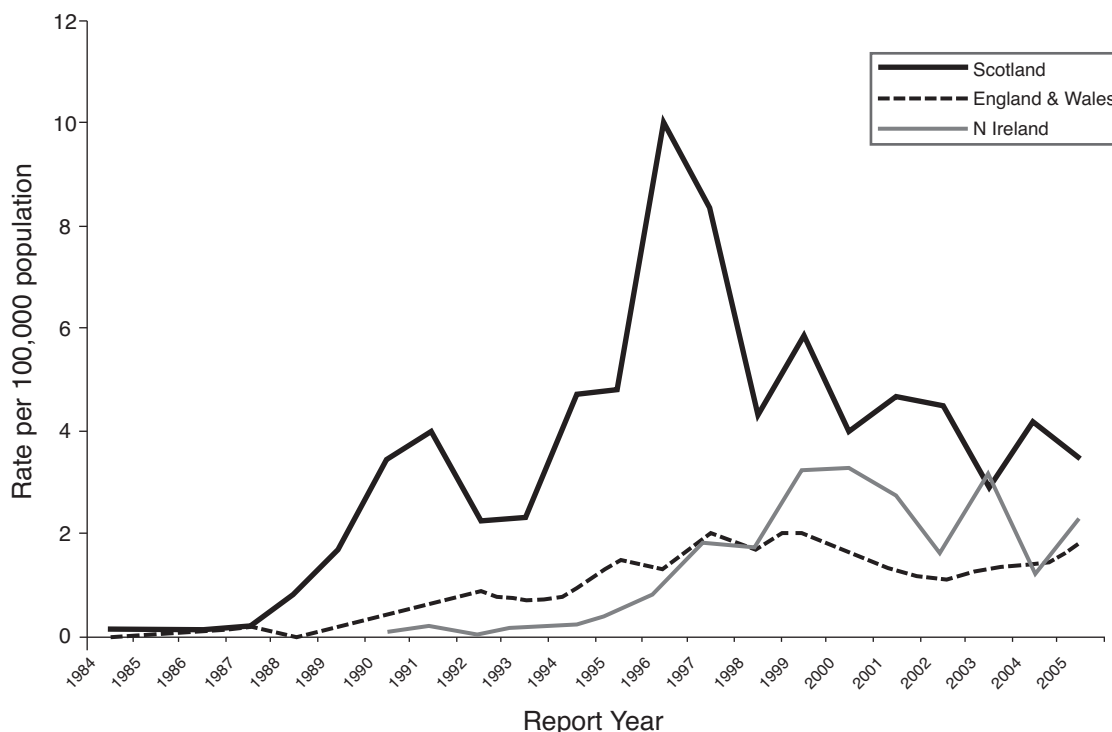


FIGURE 1. Incidence of *E. coli* O157 Infection in Scotland Compared with England and Northern Ireland (1984-2005)