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STATE OF THE ART REVIEW

Renal Failure in the Recent 2011 *Escherichia coli* O104:H4 Outbreak: A Summary on Up-to-Date Data

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Abstract

The recent 2011 *Escherichia coli* outbreak in Europe is considered as one of the biggest *E. coli* outbreak in the modern medical history. Although the induction of renal impairment is well described in *E. coli* infection, the specific knowledge on *E. coli* O104:H4 is very limited. To add up to known knowledge, the author hereby summarizes up-to-date information on renal failure among patients in 2011 *E. coli* O104:H4 outbreak.

Keywords: *Escherichia coli* O104:H4, renal failure, outbreak

INTRODUCTION

The recent 2011 *Escherichia coli* outbreak in Europe is considered as one of the biggest *E. coli* outbreak in the modern medical history. Beginning in May 2011 in Germany, the pandemic was seen within a few weeks in several countries.^{1,2} Thousands of infected patients and many deaths were reported.^{1,2} An important cause of death is the renal problem.

Indeed, the *E. coli*-induced renal failure is an important complication of *E. coli* infection.

Although the induction of renal impairment is well described in *E. coli* infection, the specific knowledge on *E. coli* O104:H4 is very limited. To add up to known knowledge, the author hereby summarizes up-to-date information on renal failure among patients in 2011 *E. coli* O104:H4 outbreak.

EPIDEMIOLOGY OF RENAL FAILURE AND HEMOLYTIC UREMIC SYNDROME PROBLEM IN THE RECENT 2011 *E. COLI* O104:H4 OUTBREAK

Renal involvement is not uncommon among the patients hospitalized with infection.^{3–5} About one-quarter of the patients developed acute renal failure.^{3–7} Of interest, hemolytic uremic syndrome (HUS) is an important complication that can be seen in many patients in 2011

E. coli O104:H4 outbreak. Indeed, HUS in *E. coli* O104:H4 infection is not a new thing. According to the literature searching in the data, there was a report from Korea before the 2011 *E. coli* O104:H4 outbreak.⁸ In the *E. coli* O104:H4 outbreak, almost all patients with renal failure ended up with HUS within 1 week after the onset of diarrhea.^{3–7} Patients of any age group or sex take the similar risk of developing acute renal failure and HUS.^{3–7} Focusing on the mortality, the death rate of the patients with HUS is about 4%.⁹

CLINICAL ASPECTS OF RENAL FAILURE IN THE RECENT 2011 *E. COLI* O104:H4 OUTBREAK

As noted, acute renal failure can be seen in a large portion of the patients in the recent *E. coli* O104:H4 outbreak. The patients usually have bloody diarrhea and the clinical picture of acute renal failure or HUS (characterized by acute hemolytic anemia, thrombocytopenia, and renal insufficiency) can further develop similar to classical enterohemorrhagic *E. coli* infection.¹⁰ For definite diagnosis, stool culture and serological testing is useful to identify the cause of the disease and renal function test is an additional tool to diagnose renal failure.¹¹ However, identification of the exact serotype is more useful for epidemiological aspect than therapeutic aspect.

Focusing on the treatment of *E. coli* O104:H4 outbreak, antibiotic treatment is not recommended because it cannot reduce the duration of the disease.¹⁰ It is reported that the pathogen is highly resistant to third-generation cephalosporins showing extended-spectrum β -lactamases resistance property.^{11,12} Sometimes, the use of antibiotics can result in unwanted negative complications.¹⁰ In addition, antimotility agents and nonsteroidal anti-inflammatory drugs should not be prescribed. To manage the renal problem, fluid therapy is required. In patients with HUS, management of the hematological complications of HUS, monitoring for extrarenal involvement, and fluid supportive treatment are required. The effectiveness of the standard renal failure treatment is confirmed; however, additional management is usually required for the patients with HUS.^{10,11,13} Plasma exchange therapy is an interesting approach. According to the report by Colic et al.,¹² plasma exchange could be successfully used for management of HUS. Improvement of renal function, platelet count, and neurological status could be obtained after exchange and the patients can be discharged at 1 week after therapy.^{11,14} Another interesting treatment is the use of complement-blocking antibody (eculizumab).¹⁵ This has proved to be effective but has not been well studied on some specific groups of patients, especially for the pediatric patients.¹⁵

Finally, an interesting therapeutic approach is immunoadsorption.^{16,17} This method is proved for its effectiveness in the reduction of renal and neurological disorders in patients with HUS and is suggested for patients for whom other therapeutic choices have failed.¹⁶ If good management is provided, follow-up of the patients usually reveals complete recovery.¹¹⁻¹⁹

PATHOBIOLOGY OF THE PATHOGEN IN THE RECENT 2011 *E. COLI* O104:H4 OUTBREAK

In the recent 2011 *E. coli* O104:H4 outbreak, the focused problematic pathogen is *E. coli* O104:H4. The renal failure and HUS in 2001 *E. coli* O104:H4 outbreak is due to Shiga toxin, which is an inducer of apoptosis of renal cell and inflammation, producing property of the pathogen.²⁰⁻²² Based on a recent molecular microbiology on the isolates in the outbreak, it is found that all isolates have "virulence profiles combining typical Shiga-toxin-producing *E. coli* (stx(2), iha, lpf(O26), lpf(O113)) and enteroaggregative *E. coli* (aggA, aggR, set1, pic, aap) loci."²³ This confirmed the nature of Shiga toxin-producing property of the pathogen.²³ However, the important significant differences from other strains are the identification of a prophage-encoding Shiga toxin 2 and antibiotic resistance factors.²⁴⁻²⁷ These mentioned properties are the points used in molecular diagnosis for discriminating between the outbreak strain and other strains.^{28,29} Tracing back to molecular technology, it can be seen that

the problematic 2011 *E. coli* O104:H4 strain evolved from enterohemorrhagic *E. coli* O104:H4 progenitor passing, getting, and losing both chromosomal and plasmid-encoded virulence factors.³⁰⁻³²

PREVENTION OF RENAL FAILURE: LEARNING FROM 2011 *E. COLI* O104:H4 OUTBREAK

As noted, the renal failure is a common complication in patients in the recent outbreak. Therefore, a big question is how to prevent such an episode. Basically, the prevention of infection can be the first thing.³³ This is totally effective. But in case that infection has already occurred, a good follow-up of the patient is required.¹¹⁻¹⁹ Recognition of the fact that the renal problem is common and can be easily seen in a short period brings the need for good fluid management and early hospitalization of the patients presenting with severe bloody diarrhea.³³⁻³⁵ Early dialysis in patients with significant rapid impairment can be a good tool for prevention of severe clinical outcomes.¹⁵

CONCLUSION

Renal failure is a common problem in the recent 2011 *E. coli* O104:H4 outbreak. The molecular characteristic of the pathogen results in the high rate of renal failure in the affected patients. HUS is common and can result in high mortality. The basic renal failure management in addition to some specific treatment is required for management of the severe cases.

Declaration of interest: The author reports no conflicts of interest. The author alone is responsible for the content and writing of the paper.

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