Policy Review

Epidemiology and Pathogenesis of *C. difficile* and MRSA in the Light of Current NHS Control Policies: A Policy review

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Abstract

Healthcare associated infections (HCAIs) cause significant morbidity and mortality, and are estimated to cost the United Kingdom National Health Service £1 billion annually. The current health care infection rates suggest that the level of performance to avoid HCAIs is not maintained consistently. Increasing screening, improving local accountability and performance management, careful use of antibiotics in the management of emergency patients, health economy wide approaches, and improved hand washing will be effective in lowering the rate of HCAIs. This paper reviews current NHS Control Policies in place for Methicillin Resistant Staphylococcus Aureus (MRSA) and *C. difficile*.

Introduction

Heath care associated infections (HCAIs) are infections acquired during treatment for some other conditions within the health care settings. HCAIs can occur in hospitals, nursing homes, and primary care settings. The infection can be transmitted from patient to healthcare provider, or vice versa. Infections can also be transmitted between patients and healthcare providers.[1] The current health care infection rates suggest that the level of performance used to avoid HCAIs is not maintained consistently. This could be due to staff shortages, bed shortages, and skill mix.[2] On average, HCAIs add 11 days to the length of stay for each affected patient. Around 320,000 HCAIs occur every year (approximately 3 million during the last decade). HCAIs are estimated to cost the United Kingdom National Health Service (NHS) £1 billion annually. Around a third of HCAIs can be controlled by reducing the spread of infection in healthcare settings.[3]

Methicillin Resistant Staphylococcus Aureus (MRSA)

MRSA is caused by *Staphylococcus aureus* (*S. aureus*) bacteria.[4] It is a gram-positive, non-motile, spherical, anaerobic bacterium that can grow at a temperature range of 15–45 degrees Celsius.[5] It is found in the nose, throat, mucous membranes, and on the skin of humans (such as the perineum, groin and axillae), often harmlessly. 40% of *S. aureus* infections are now due to MRSA.[6]

Pathogenesis

Methicillin was first introduced in 1959–60 and in just one year (1961), methicillin-resistant isolates were reported in the UK. Healthcare associated MRSA (HA-MRSA) infections were historically caused by internationally scattered multi-drug-resistant clones including the Iberian, Brazilian, Hungarian, New York/Japan, and Paediatric clones. The spread of these five major clones was responsible for the majority of the MRSA infections in many regions.[7]

MRSA is a potential pathogen of humans, and one of the major causes of infection in hospitals and other health care settings such as nursing homes and dialysis centres. The host response to MRSA infection may include inflammation, boils and pus-filled lesions as well as systemic malaise. In MRSA infection, *S. aureus* develops resistance to Beta-lactam producing antibiotics through synthesis of penicillin-binding protein 2a (PBP2a). PBP2a has a low affinity for Beta-lactams allowing for transpeptidase activity and cell wall synthesis.[8] As a result the bacterium continues to grow and reproduce. This results in patient colonisation and infection, ranging from mild to life threatening. The immune response is disrupted in MRSA infection and this results from *S. aureus* sticking to different tissues in the body. Additionally, it can produce a protein that attacks white blood cells, interfering with their function during the immune response. The bacteria can also cause tissue

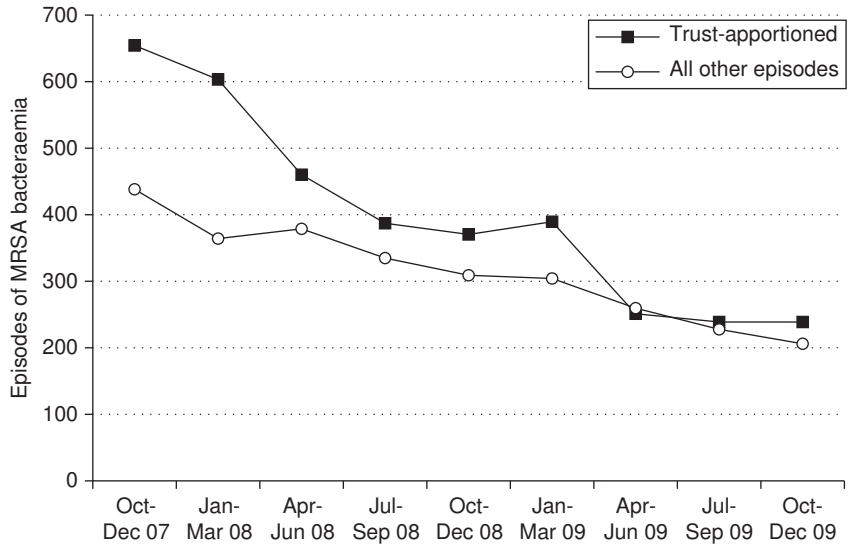


Fig 1 Trust-apportioned and all other episodes of MRSA.

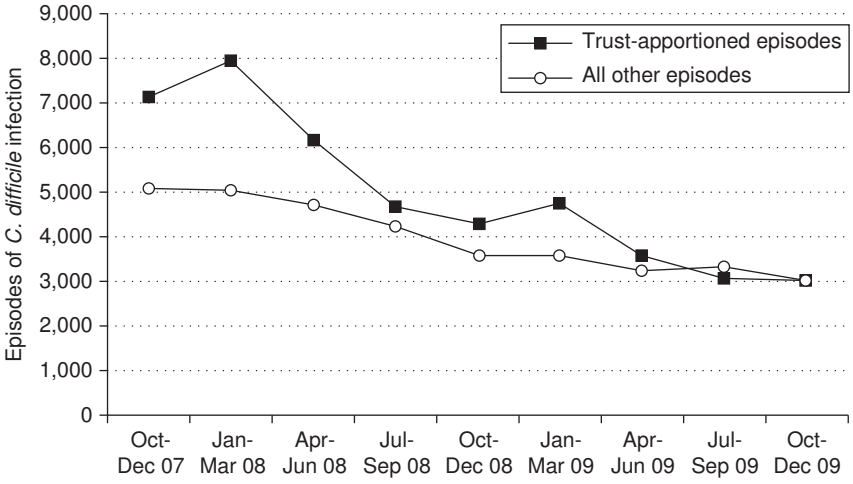


Fig 2 Trust-apportioned and all other episodes of *C. Difficile*.

destruction by producing a toxin which acts as a super-antigen; this can lead to septic shock. In the hospital setting, the bacteria can cause a bio-film on the surface of instruments, such as catheters and prosthetic devices, making it resistant to antimicrobial agents.[9] Serious complications can occur when the bacteria enters the blood stream. MRSA infections can be divided into two parts on the basis of its acquisition (Figure 1)[10]:

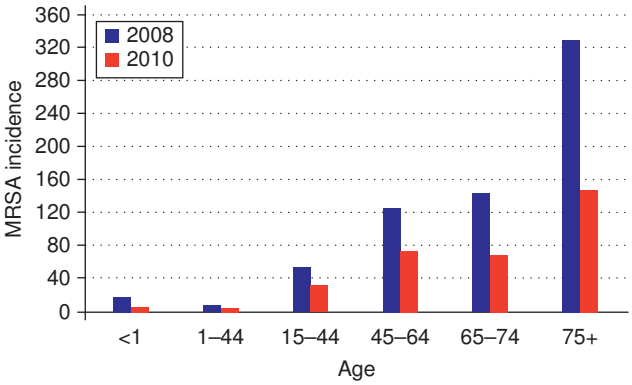
- Trust-apportioned infections: Presumed to have been acquired in hospital.
- Primary care organisations (PCO) infections: Presumed to have been acquired outside the hospital.

The mode of transmission of MRSA is mainly from colonised (the presence and multiplication of MRSA on the body without any host response) or infected (deposition and multiplication of MRSA with an associated host response) patients to others, via hands or equipment. It is also transmitted when a healthcare worker touches patients who are MRSA carriers and don't wash their hands between interactions. The portal of entry of MRSA can be a hair follicle, break in the skin, or the respiratory tract. Foreign bodies such as sutures, breathing tubes and catheters can readily get colonised by bacteria; making it difficult to control the infection. The incubation period between the transmission of the bacteria and the onset of signs and symptoms of infection is 1–10 days on average.[5] The individual remains infectious until they are no longer colonised by the bacteria.

MRSA infections are not generally more serious than *S. aureus* infections. The spread of MRSA infection can be avoided by isolation of infected patients, hand washing, prompt antibiotic treatment, and increased awareness of the disease. However, the resistance to antibiotics in MRSA makes it more difficult to treat. *S. aureus* infections are normally treated with penicillin-like antibiotics. But due to resistance developed by MRSA bacteria, it is now treated with other antibiotics (e.g. Vancomycin).[11] Vancomycin can only be administered in the hospital; it is expensive

Table 1 Rates of MRSA bacteraemia in English NHS Trust April 2007 to March 2012

Financial Year	MRSA Bacteraemia Reports	MRSA bacteraemia rate per 100,000 bed days
2007–8	4,451	11.9
2008–9	2,935	7.8
2009–10	1,898	5.1
2010–11	1,481	4.2
2011–12	1,114	3.2



Source: HPA, 2011

Fig 3 MRSA incidence by age comparison between trusts and non-trusts, England and Wales, 2008–2010.

with some reported side effects such as nausea, hypertension, chills, fever, renal failure, intestinal nephritis, and ototoxicity.[12]

Epidemiology

There was a significant increase in the rate of HA-MRSA for the past 20 – 30 years.[13] However, data from the Health Protection Agency shows that the rate of hospital acquired MRSA bacteraemia has declined in England in the last five years (Table 1).[14] This indicates that the NHS is continuing to make progress in reducing the number of cases .

In Europe, the UK has the highest rate of MRSA infection, with hospitalised patients most at risk. The infection rate varies between hospitals and specialities. The spread of infection is higher in intensive care and high dependency units, additionally neonatal units and orthopaedics also show high spread of infection. In contrast, minimal risk is found in mental health units and outpatient departments.[10] MRSA is more common in immune-suppressed adults, particularly the elderly, but the rate has significantly increased in children over the past few years (Figure 3).[26] In 2009, 48% of cases were reported in those aged 75 years or more in the UK. Around 5,000 people die from MRSA blood infections each year. In 2005–2009, 621.7 deaths per million in males and 307.3 deaths per million in females were reported. However, the death rates have decreased for both males and females since then.[25] It is a major public health problem in the context of an ageing society,[15] with hospitalised elderly patients being more vulnerable through co-morbid conditions and malnourishment[16] and hence may not have sufficient physiological reserve to deal with the infection. Thus, more minor infections can become severe and fatal in some cases.

In England, there has been a 59% reduction in the incidence of MRSA cases between 2007 and 2009. 1,092 cases (654 cases of trust acquired + 438 cases of non-trust acquired) were reported between October and December 2007. Over the same period in 2009, only 444 cases (237 cases of trust acquired + 207 cases of non-trust acquired) were reported. Therefore, there has been a 64% reduction in hospital acquired, and 53% reduction in community acquired, MRSA. However, no significant change was reported in trust acquired cases from April to December 2009. The control of the spread of infections from MRSA is therefore necessary for safe patient care.[17]

Measures to fight HCAIs need to be strengthened. All relevant emergency admissions in the hospital must be screened for MRSA carriage irrespective of their route of attendance (A&E, Minor Injuries Unit, GP, or outpatient clinic).[21]A patient known to be colonised or infected with MRSA, or from another hospital or country where MRSA is a major problem (e.g. Austria, Australia, Germany,Greece, France, Ireland, Italy, Middle and Far East, South Africa, Spain,) should be placed in a side room and isolated until a full MRSA screen is carried out. The infection prevention and control team (IPCT) should be contacted if a patient is MRSA positive. This strategy will help reduce the spread of infection to other patients. Three full sets of swabs (either from the nose, perineum, axillae, skin lesions, wound sites, sputum, throat or umbilicus) are required to ascertain MRSA status.[18] Until the swab results are ascertained, the suspected high-risk patient must be treated as positive for MRSA. Patients discharged before screening results return should be contacted and offered suppression therapy by the hospital or GP if they test positive for MRSA.[18] If MRSA is suspected in the swab, the bay should be closed and no further patients should be admitted into the bay. The infected patient should continue to be isolated in a side room. Contact screening of any patient in contact with the affected patient for more than 24 hours should be carried out. The MRSA status, care plan, and isolation procedure should be clearly documented in the patient notes. A repeat screening procedure should be carried out when transferring the patient to the main ward, as well as when discharging them.[19]

Gloves and aprons must be worn when giving direct patient care. Hospital staff must wash their hands with liquid soap thoroughly (or use alcohol hand rub) after any procedures.[20] Relatives and visitors must be asked to wash their hands (or use alcohol gel) before and after contact with the patient. The number of people entering the patient's room must be minimised; those entering should be advised of the necessary precautionary measures. Patients must be informed of the reason for isolation precautions. However, visitors must be reassured that there is no risk to healthy relatives or others outside the hospital.[21]

Staff should ensure that an apron and gloves are worn before entering the patient's room and thorough hand washing is carried out before leaving the patient's room to reduce the risk of transient carriage. Temporary staff providing care to the MRSA patients must shower and change their uniforms before starting their next shift.[22] Equipment such as X-ray machines, wheelchairs, walking aids, and ambulance

or patient trolleys used by the patient must be cleaned with detergent and water. Theatre staff must be informed of the risk of infection well in advance so sufficient preparations can be made.[23] Patients with MRSA are generally listed last on an elective operating list to prevent cross contamination. The patient's room must be cleaned with detergents (using hypochlorite agent if required) on a daily basis, as MRSA is harboured in dust and dirt. All waste and used disposable items must be disposed of in a yellow clinical bag. Complete linen change should be done on a daily basis to prevent the organisms' dispersal into the environment. After discharge, or transferring the patient, the curtains, mattress, wardrobes, lockers, beds, and all horizontal surfaces must be cleaned thoroughly with detergent.[24] Increasing the awareness of staff has become a priority and this has led to initiatives like "Clean Your Hands" an integrated campaign used to boost hand hygiene among the staff.

Clostridium Difficile (C. Diff)

C. Diff bacteria are important HCAIs, especially in patients on antibiotics, characterised by adjustments in the patient's normal gut flora. It is a gram-positive anaerobic bacterium. It disrupts the normal flora of the colon resulting in mucosal damage, inflammation, and diarrhoea. This culminates in the condition pseudomembranous colitis.[25]

Pathogenesis

C. Diff belongs to the genus clostridium. It has been isolated from the dung of large animals, soil, faeces, hay, and sand. It is a human pathogen recognised as the major cause of antibiotic associated diarrhoea in 1978.[26] The mode of transmission of infection is through the faecal-oral route. It occurs after antibiotic therapy in an individual increases the susceptibility of infection in the gut. *C. Diff*, after colonisation, produces two principle toxins, namely enterotoxin A and cytotoxin B, that can cause diarrhoea and eventually lead to a life-threatening pseudo-membranous colitis leading to death in some cases.[27] The toxins secrete protein-rich exudates that contain neutrophils, monocytes, and sloughed enterocytes. *C. Diff* remains in the environment for a long period of time because of its ability to produce spores, making it difficult to eradicate them from the environment and to control.[27] The spores are found on commodes, toilets, wheelchairs, floors, sinks, and linen used by the infected patients. The incubation period of *C. Diff* is 1–10 days on average. They are resistant to disinfectants, air, drying, heat, and alcohol hand-rub; therefore, hands must be washed with soap and water. It requires chlorine containing products to remove the spores. Hand hygiene is required to control its spread.[28]

Primary *C. Diff* infection is triggered by the use of antibiotics prescribed to treat another condition, resulting in a change in normal gut flora and predisposition to *C. Diff* infection. Secondary infection is associated with the ingestion of the spores of the bacteria from the environment (possibly due to a nearby primary infection and cross contamination via healthcare staff). In primary infection, currently prescribed antibiotics should be discontinued or changed to oral Metronidazole or Vancomycin. The patient is considered to be infected with the organism during the diarrhoeal episode. Due to the explosive nature of the diarrhoea, contamination of the patient, equipment, or environment may occur. This can result in faecal-oral transmission on the hands of healthcare workers when dealing with the patient and their equipment.[29]

Table 2 Rates of Clostridium Difficile infection 2007–10

Year	PCO Attributed Rate	Trust Apportioned Rate
2007/08	11.1 cases per 10,000 population	9.3 per 10,000 bed days
2009/10	5.1 per 10,000 population	3.6 per 10,000 bed days

Epidemiology

The risk of *C. Diff* infection increases in the elderly, possibly due to a less effective natural barrier to infection, with double the number of cases for 85 year olds and above compared to 75 – 84 year olds. It affects more females than males. In England, there has been a 58% decrease in trust acquired cases and 41% decrease in all the other cases between the period of October to December 2007 and the same period in 2009 (Table 2). In 2009–10, a total of 25,604 cases of *C. Diff* were reported whereas in 2010–11 there were 36,095 reported cases, a 29% reduction. This could be attributed to healthcare workers, and patients' visitors, using the appropriate guidelines put in place by the Department of Health. The mortality rate of *C. Diff* has also reduced from 5,931 in 2008 to 3,933 in 2010.[30]

Antibiotic therapy is used for the treatment of infection with *C. Diff*. However, in some cases (mainly in old age groups) the symptoms reappear due to prolonged use of antibiotics and long stay in the hospital. The patient must be isolated in a side room, preferably with en-suite toilet facilities, to avoid the spread of the infection. At the same time, IPCT (required to institute effective isolation of the patient) and a microbiologist (to confirm the outbreak) should be contacted and the bay must be closed for further entries. The toilet must be positioned close to the hand wash basin to facilitate hand washing.[31]

A chlorine-releasing detergent should be used when cleaning the environment from spillage or soiling. The patient, staff, and visitors must be informed to wash their hands thoroughly with soap and water as alcohol based hand gels may not kill the spores of *C. Diff*.[30] Hand washing must be performed after handling the patient, bed pans, commode, or other soiled equipment. Gloves and an apron should be worn by staff when entering the patient's room. If the diarrhoea reappears after shifting the patient to the ward, the patient should be screened again and isolated until the results are obtained.[32]

To identify cross-infection, reduce transmission, optimise management of outbreaks, and determine the epidemiology of *C. Diff*, the *Clostridium difficile* Ribotyping Network (CDRN) for England and Northern Ireland was set-up.[33] The Health Protection Agency (HPA) surveillance results on CDRN revealed that only 13% of patients with one episode of *C. Diff* infection had reported a repeat episode in 180 days of follow-up. In 2008/09 one in every eight cases of *C. Diff* infection were examined by the CDRN which has now increased this rate to one in every four or five cases in 2009/10, in England. This data shows a significant reduction in the number of these infections in the NHS.[31] Other technologies to reduce infection include assessing the efficacy of automated washer disinfectors, and the better cleaning of surgical instruments. In laboratories and in sterilising departments of hospitals the

thermostableadenylate kinase (tAK) technology is being used to prevent the spread of infection.

Conclusion and Recommendations

Khairulddin et al.[34] have shown the negative impact of the economic downturn on hospital performance particularly cancer waiting times and HCAIs like MRSA and *C Diff*.[35] Measures such as increasing screening, improving local accountability and performance management, careful use of antibiotics in the management of emergency patients, health economy wide approaches, reducing infections in low rate areas such as elderly/medical care will be significantly effective in bringing the rate of HCAIs down.[36]

Ethical approval

No ethical approval required for this study.

Conflict of interest

No conflicts of interest have been declared by the author.

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