Experience of transmissible carbapenemase determinants (TCDs) from a UK tertiary paediatric hospital: Great Ormond Street hospital

Lucey, O., Dunn, H., Asadi, F., Hartley, J.

Microbiology department, Great Ormond Street Hospital, London, WC1N 3JH

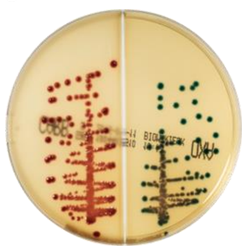
Introduction

The emergence and spread of TCDs among gram negative bacteria has become a major source of global health concern. Limited data is available on detection and screening of TCDs in paediatric populations. Great Ormond Street Hospital is a large tertiary paediatric centre attracting a mix of complex national and international patients. There are large cardiothoracic, haematology, oncology and transplant facilities with patients often requiring multiple admissions both at this centre and other local hospitals within and outside the UK. There is no routine screening for carbapenemase-producing enterobacteriaecae (CPE) in the UK. The Public Health England (PHE) toolkit suggests that patients should be assessed on admission for risk of colonisation or infection and isolated and screened accordingly. Local policy at GOSH is to perform routine faecal screening on all admitted patients. Carbasmart selective plates were introduced to enhance faecal screening from January 2015.
We aimed to understand the trends in prevalence and epidemiology of TCDs in this paediatric population and evaluate faecal screening for rapid detection of TCDs.

Methods

All isolates harbouring TCDs identified at GOSH and confirmed at the reference laboratory between 2002 and 2017 were reviewed. Isolates were identified from faecal screens or clinical samples. Between 2002 and 2004 any gram negative organism identified from high risk patients (i.e. BMT/haem/onc/immunology) on faecal screens or any gentamicin resistant gram negative organism from routine non-high risk faecal screens was followed up to identify the resistance mechanism. Between 2004 and January 2015, a meropenem disc was added to MacConkey plates for all faecal screens to increase sensitivity. As part of the enhanced faecal screening programme, selective carbapenemase plates (CHROMID® CARBA SMART selective chromogenic media bi-plate) (see Fig 1) were introduced in January 2015. These plates are incubated at 35-37ºC in 5-10% O_2 for up to 24 hours. They are designed to promote growth of OXA-48 producing organisms on one side and other TCDs e.g. KPC and NDM-1s on the other. Any possible TCD i.e. a gram negative organism growing from the carbasmart plate or isolate with reduced sensitivity to carbapenems or high level temocillin resistance is identified using MALDI-TOF and appropriate sensitivities set up, with the use of meropenem and imipenem MICs and ROSCO kits as necessary according to SOP. The side of the carbasmart plate with the growth of the isolate was documented.

Figure 1



We audited faecal screening compliance for all admissions since January 2015 by reconciliation of laboratory and admission data using SQL (Structured Query Language).

Results

A total of 100 isolates amplified one or more TCD genes in 92 patients. 70% of TCDs were identified through faecal screening (see figure 2).

Table 1

Age		
<12 months	28	30.4%
12 - 23 months	20	21.7%
2 - 5 years	19	20.7%
6 - 10 years	12	13.0%
11 - 18 years	13	14.1%
Sex		
Female	39	42.4%
Male	53	57.6%

Table 2

Provenance (in first time isolates)		
Home	48	52.2%
Hospital - NHS	24	26.1%
Hospital - private	9	9.8%
Outpatient	5	5.4%
Temporary residence	6	6.5%
Previous contact with GOSH		
Yes	54	58.7%
No	38	41.3%
Residency		
London	20	21.7%
Essex	16	17.4%
Middlesex	6	6.5%
Home counties	9	9.8%
UK (other)	4	4.3%
Europe (Malta, Portugal, Cyprus, Macedonia, Ireland)	9	9.8%
Middle East (Kuwait, UAE, Oman, Doha, Bahrain, Saudi, Qatar, Jordan, Iran, Egypt)	24	26.1%
South Asia (India, Pakistan)	2	2.2%
Other (Nigeria, Venezuela)	2	2.2%

Tables 1 and 2 describe the demographics and epidemiology of the patients colonised or infected with TCDs.

- 52.1% of patients with TCDs were under 2 years old when their first isolate was identified at GOSH.
- 26.1% of patients lived in the Middle East whilst 37.1% lived in London or Essex.
- 58.7% of patients had either been admitted or seen in outpatients at GOSH previously before the identification of their first TCD isolate

Figure 2

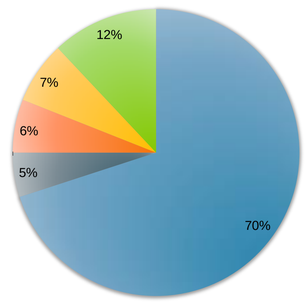


Figure 3

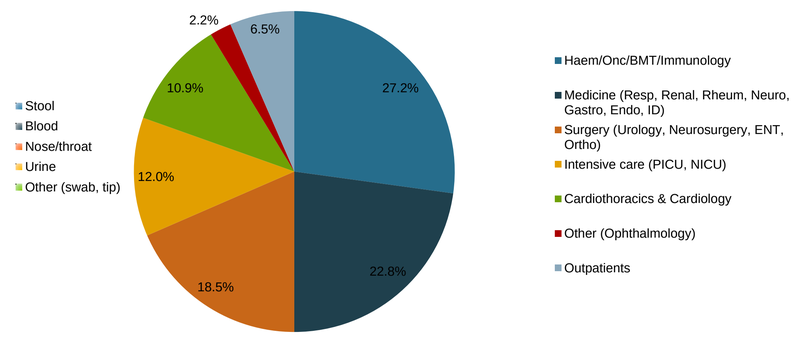


Figure 3 demonstrates the main specialty to which the patient was admitted or seen by at the time of the first positive isolate. Half of the TCDs were isolated from patients under haematology, oncology, BMT and medical specialties.

Figure 4

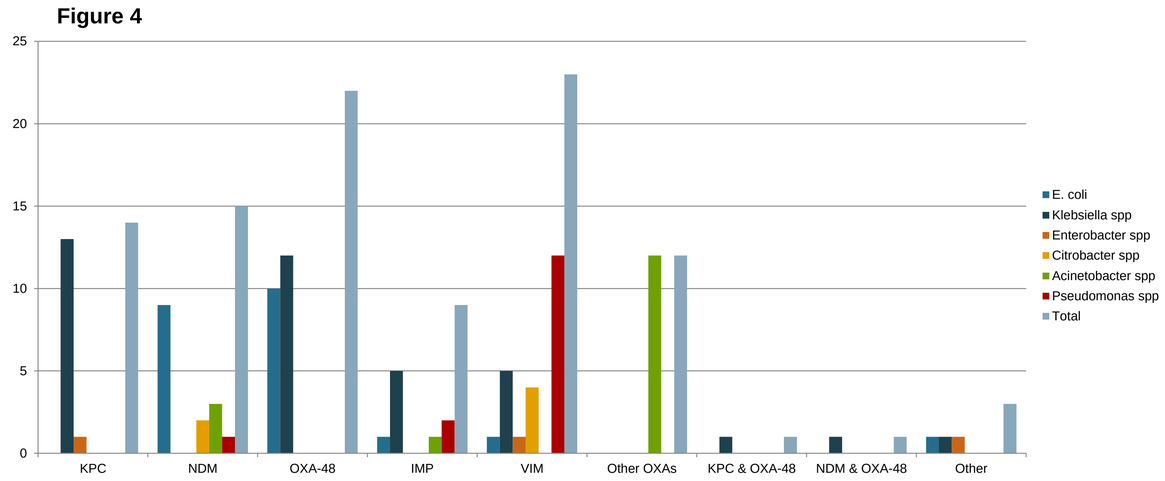
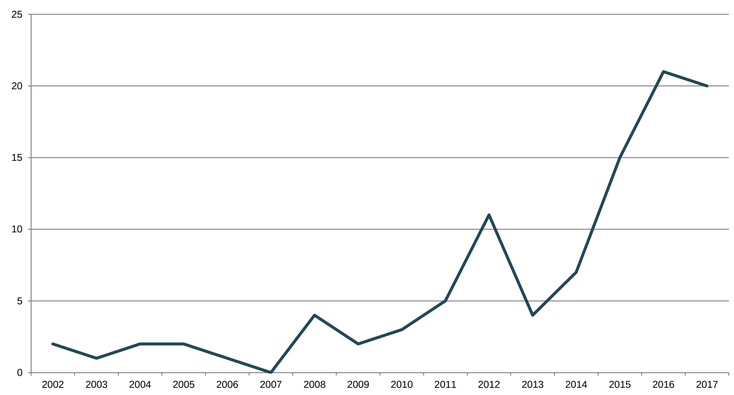


Figure 4 demonstrates the types and numbers of TCDs and to which organism they pertain. The majority of isolates identified contained blaOXA-48 (24 specimens), blaVIM (23), blaNDM (16) or blaKPC (15). The most common organism to harbour a TCD was Klebsiella (38), then E coli (22) followed by Acinetobacter (16) and Pseudomonas (15). This highlights the importance of including acinetobacter and pseudomonas in terminology and detection methods.
Figure 5 demonstrates the increasing trend in TCD detection between 2002 and 2017.

- 56% of the total TCDs were isolated since January 2015
- 29.2% of TCDs isolated through faecal screening since January 2015 were detected through growth on the carbasmart plate only and therefore would have been missed using laboratory methods prior to 2015.
- Laboratory notes were unavailable for 20% of these TCDs suggesting that possibly up to 50% of isolates would not have been detected using older methods.

Figure 5



Interestingly, since January 2015 only 31.4% of patients admitted (>48 hours) had a faecal screen within 72 hours of admission. Despite this poor screening compliance, 56% of all TCDs since 2002 were identified after the introduction of the carbasmart plate in January 2015 demonstrating a significant increase in detection rate. Importantly, 60% of faecal isolates would not have met the PHE criteria for isolation and testing.

Conclusions

GOSH has seen a significant increase in TCDs since 2002, particularly since 2015. Our data suggests this is due both to increased incident cases in line with global trends, and increased detection with enhanced laboratory methods. Due to the complex nature of GOSH's caseload there is an argument for routine faecal screening in such populations. Our data suggests PHE criteria for isolation and testing risks missing a large number of patients harbouring TCDs.

Bibliography

1. Logan L, Weinstein R. **The epidemiology of Carbapenemase-Resistant Enterobacteriaceae: The Impact and Evolution of a Global Menace**. *J Infect Dis. 2017 Feb 15;215(suppl1):S28-S36.*
2. Logan L. **Carbapenem-Resistant Enterobacteriaceae: An Emerging Problem in Children.** *Clin Infect Dis.2012 Sep;55(6):852-9.*
3. Nordmann P, Naas T, Poirel L. **Global Spread of Carbapenemase-producing *Enterobacteriaceae.*** *Emerg Infect Dis. 2011 Oct; 17(10): 1791–1798.*