

# Longitudinal survey of ATB resistance reversibility in children with AIDS of genocide survivors in Cambodia

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Original Articles

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## Key words:

HIV, AIDS, antimicrobial resistance.

## Key message:

ATB, resistance in HIV positive children is reversible.

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## Abstract:

**Background:** The aim of the survey was to assess antimicrobial resistance dynamics and reversibility in the group of children with AIDS in Cambodia in 2003 - 2015.

**Patients:** Correlation between antimicrobial (ATB) resistances in commonest respiratory isolates among 140 children with AIDS on antiretroviral therapy was studied from 2003 to 2015 in 586 isolates.

Results: All but 3 (98%) children showed a sustained CD4 increase after introduction of antiretroviral therapy (ART) followed by a decrease of ATB resistance. In our group of children restoration of the immune system decreased the number of infection diseases episodes and the proportion of multi-resistant bacterial strains.

Conclusions: Less frequent use of antimicrobial therapy probably led to the decrease of multi-resistance and restoration of susceptibility of studied respiratory bacterial isolates.

## Introduction

Reversibility of ATB resistance has been described on both countrywide and hospital level (1-3), however specific patient groups have been rarely addressed in adults with HIV or Ebola in Sub-Saharan Africa (4-5). Antibiotic resistance is of great concern in patients with AIDS, who are frequently treated with antivirals, antibiotics and anti-tubercotics for various opportunistic infections. After the introduction of highly active antiretroviral therapy in 1990/2000 most opportunistic infections (OI) decreased. Therefore, also the amount of prophylactically and therapeutically administered antibiotics decreased. Because the amount of antibiotic agents is one of the drivers of ATB resistance, also resistance to antibiotics and anti-tubercotics should decrease. The aim of this longitudinal research is to determine if resistance of commonest respiratory agents have decreased after the implementation of ART in children in community settings.

## Patients and methods

This longitudinal study includes 12 years (2003-2015) follow up of susceptibility to antibiotics of upper respiratory tract isolates from nose and pharyngeal swabs in children 4-12 years on HAART. 98% of children showed CD4 increase within 6 months on ART to normal level  $> 25\%$  or  $> 350/\text{mm}^3$ ). In the statistical analysis, t-test for trends was used to compare ATB resistance in 2003 to 2015 (EPI INFO version 2014).

## Results and discussion

**Table 1** presents trends in ATB resistance in major respiratory isolates from October 2003 to December 2015 (total of 586 isolates). Penicillin resistance in pneumococci decreased from 25% to 2% in 2015 ( $P < 0.01$ ); t-test for trends), MRSA from 33.3% in 2003 to 3% in 2014 and 2% in 2015 ( $P < 0.01$ ). Erythromycin resistance in *Streptococcus pyogenes* decreased from 10.5% in 2003 to 3.3% in 2015. At baseline extremely high proportion of ESBL - producing Enterobacteriaceae decreased from 66.6% to 25% and such trend was also observed in *Candida* species and resistance to fluconazole (from 15% in 2003 to 6% in 2015).

Reversibility of ATB resistance was documented on the hospital level (2) or on the community national level (1,3), however only in countries with small population (Finland, Denmark, Iceland) with centralized ATB policy. Reversibility time was 2-5 years per country and more (up to 5 years). Reversibility of susceptibility or antibiotic resistance was not yet sufficiently studied in pediatric population with specific immunodeficiency therefore it is deficient to assess, of 10 - 15 years in our group is comparable to e.g. 2 - 5 years on a nation level from Europe (5-8).

## Conclusions

A decrease of the MRSA, PRP, and ESBL producing Enterobacteriaceae and FLU-R in *Candida* species is in correlation with improved immune status of children with AIDS. Restoration of the immune system with ART led to the CD4 increase and

was logically followed with less HIV related infections (4). Less antimicrobial agents use is possibly responsible for the phenomenon of the reversibility of antimicrobial resistance also in pathogens colonizing in the respiratory tracts of children with HIV on active antiretroviral therapy.

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**Tab. 1** Antimicrobial resistance pathogens among bacteria colonizing the respiratory tract in Cambodian children with HIV.

| N=586                                     | 2003 | 2004 | 2005 | 2006 | 2007 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|------|------|------|------|------|------|------|------|------|------|------|------|
| St. pneumoniae                            | 25   | 15   | 25,7 | 21,5 | 35,5 | 15,8 | 4,3  | 2,2  | 2,4  | 2,0  | 8    | 2,0  |
| MRSA                                      | 33,3 | 18,5 | 25,7 | 23,1 | 35,5 | 56,6 | 19,1 | 45,1 | 18   | 20,0 | 3,0  | 2,0  |
| Mocca                                     | 12   | 12,3 | 7,3  | 7,7  | 4    | 5,3  | 3,2  | 4,4  | 3,3  | 5,0  | 3,3  | 3,3  |
| HAIN                                      | 8    | 4,6  | 5,8  | 12,  | 0,8  | 0    | 1,1  | 1,1  | 2,5  | 6,0  | 4,1  | 3,3  |
| ERY-R<br>St. pyogenes                     | 10   | 10,5 | 15,3 | 10   | 12,4 | 10,5 | 8,2  | 5,5  | 4,5  | 4,0  | 5,0  | 3,3  |
| ESBL <sup>+</sup> Entero-<br>bacteriaceae | 66,6 | 42,5 | 72,5 | 55,5 | 29,3 | 35,5 | 22,2 | 25   | 24   | 30   | 33   | 25   |
| FLU-R Candida                             | 15   | 15   | 22,5 | 10,2 | 5    | 8,25 | 5,0  | 6,0  | 10   | 6    | 5    | 5    |
| CD4 (mean)                                | 55   | 121  | 182  | 201  | 198  | 355  | 320  | 406  | 350  | 370  | 401  | 395  |

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