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..................................................................................................................
Trends of Antibiotic Resistance in *Salmonella enterica* Serovar Typhi Isolated from Hospitalized Patients from 1997 to 2004 in Lagos, Nigeria

Dear Editor,

The increasing treatment failure with the empirical therapy in recent times among typhoid fever patients necessitates responsibility of medical microbiologists to assess and report the patterns of antibiotic resistance among *Salmonella enterica* serovar Typhi in our environment. A retrospective study of 274 *Salmonella enterica* serovar Typhi isolates recovered from patients whose blood and/or stool samples were brought to the Central Public Health Laboratory Services (CPHLS), Yaba, from 1997 to 2004 was conducted in order to assess antimicrobial resistance patterns of the isolates. Susceptibility to ampicillin (25 µg) chloramphenicol (30 µg), cotrimoxazole (25 µg), tetracycline (50 µg), nalidixic acid (30 µg), ciprofloxacin (20 µg) and ofloxacin (20 µg) was determined for all isolates by the disk diffusion Kirby Bauer method.1 After 1999, reference broth micro dilution methods recommended by National Committee for Clinical Laboratory Standard (NCCLS) for susceptibility testing using the established break points was adopted.2 For ampicillin and chloramphenicol, break points 8.0 and 16.0 µg/mL were used for intermediate and resistant, respectively. Tetracycline and cotrimoxazole ≥4.0 µg/mL for intermediate and ≥8.0 µg/mL for resistant was used, while nalidixic acid ≥4.0 µg/mL for resistant was used. The minimum inhibitory concentration (MIC) of ≤0.03 µg/mL was taken to be fully sensitive for ciprofloxacin and ofloxacin. For analysis in this study, both intermediate and resistant categories were considered to be resistant. *Escherichia coli* ATCC 25922 was used as control in susceptibility testing. In all, 221 *Salmonella enterica* serovar Typhi strains were resistant to at least three antibiotics given a prevalence of 80.7%. In 1997 alone, out of 29 isolates screened, 70.0% were resistant to more than three antimicrobials. This was gradually increased in the subsequent years. For example, 80.0% and 88.6% were recorded in 2000 and 2002, respectively, with a slight decrease in 2004 to 84.6% (Table). Similar trends were recorded for *Salmonella enterica* serovar Typhi with single drug resistance. For instance, in aggregates, the highest percentage of resistance was found to chloramphenicol (83.6%) followed closely by ampicillin (81.8%), cotrimoxazole (81.4%) and tetracycline (79.6%), while the least was nalidixic acid (59.0%). A strain of *Salmonella enterica* serovar Typhi with reduced ciprofloxacin and ofloxacin susceptibility was recorded in 1999 and 2004 (Table).

Therefore, the high prevalence of MDR (multidrug resistant) *Salmonella enterica* serovar Typhi recorded may be attributed to two main reasons. Firstly drug abuse, which is because of therapeutic intervention in suspected cases of typhoid fever due to attitude of self-medications. This prevents early reporting of patients to the hospitals at the onset of disease symptoms, except where complications had occurred, as observed in this study, where only untreated cases of typhoid fever by self-medication were brought to the hospitals. It should be noted that severe, refractory or complicated infections have been attributed to increase chloramphenicol and other antibiotic resistance in strains of *Salmonella enterica* serovar Typhi in some parts of the world,3 a situation that seems to have come to stay in our environment. Secondly, either clonal spread and/or extrachromosomal genes may be potential mechanisms for increase in the level of reduced susceptibility as noticed in this study, an observation that has been well documented in literature.4,5 The implication of high prevalence of multiple antibiotic resistance recorded in our study is that efficacy of the relatively cheap empirical therapy for typhoid fever patients in Nigeria is now doubtful and thus calls for urgent attention. More importantly, the increasing trends of MDR - *Salmonella enterica* serovar Typhi may spread to neighbouring countries of Africa and other parts of the world particularly among the travelers returning from this region, if the unprecedented upsurge remains unchecked. This study revealed increased circulation of MDR - *Salmonella enterica* serovar Typhi isolates over relatively short period. We suggest restriction and/or immediate stoppage, for a while, of the use of chloramphenicol and other first line antibiotics for the treatment for typhoid fever, to prevent possible emergence
of resistance strains to relatively safe antimicrobials such as ciprofloxacin and ofloxacin in Nigeria.

References


*KO Akinyemi, AO Coker

Department of Microbiology (KOA), Lagos State University; and Department of Medical Microbiology and Parasitology (AOC), College of Medicine, University of Lagos, Nigeria

*Corresponding author (email: <akinyemiko@yahoo.com>)

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### Table: Antibiotic resistance in *Salmonella enterica* serovar Typhi isolated from hospitalized patients from 1997-2004 in Lagos

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<th>Year</th>
<th>Number of isolates</th>
<th>Number of isolates resistant to each antimicrobial (%)</th>
<th>Number of MDR</th>
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<tr>
<td>1997</td>
<td>29</td>
<td>20 (70.0) 21 (72.4) 21 (72.4) 20 (70.0) 14 (42.3) 0 (0.0) 0 (0.0)</td>
<td>20 (70.0)</td>
</tr>
<tr>
<td>1998</td>
<td>37</td>
<td>28 (75.7) 30 (81.1) 26 (70.3) 30 (81.1) 16 (43.2) 0 (0.0) 0 (0.0)</td>
<td>28 (75.7)</td>
</tr>
<tr>
<td>1999</td>
<td>26</td>
<td>21 (80.0) 20 (76.9) 20 (76.9) 21 (80.0) 11 (42.3) 1 (3.8) 1 (3.8)</td>
<td>20 (76.9)</td>
</tr>
<tr>
<td>2000</td>
<td>38</td>
<td>30 (79.0) 31 (81.6) 29 (76.3) 31 (81.6) 17 (47.4) 0 (0.0) 0 (0.0)</td>
<td>30 (79.0)</td>
</tr>
<tr>
<td>2001</td>
<td>33</td>
<td>28 (84.8) 29 (87.9) 28 (84.8) 27 (81.8) 17 (51.5) 0 (0.0) 0 (0.0)</td>
<td>28 (84.8)</td>
</tr>
<tr>
<td>2002</td>
<td>35</td>
<td>31 (88.6) 31 (88.6) 30 (85.7) 30 (85.7) 20 (57.1) 0 (0.0) 0 (0.0)</td>
<td>31 (88.6)</td>
</tr>
<tr>
<td>2003</td>
<td>37</td>
<td>32 (86.5) 33 (89.2) 31 (83.8) 30 (81.1) 20 (56.8) 0 (0.0) 0 (0.0)</td>
<td>31 (83.8)</td>
</tr>
<tr>
<td>2004</td>
<td>39</td>
<td>34 (87.2) 34 (87.2) 33 (84.6) 34 (87.2) 23 (59.0) 1 (2.5) 1 (2.5)</td>
<td>33 (84.6)</td>
</tr>
<tr>
<td>Total</td>
<td>274</td>
<td>224 (81.8) 229 (83.6) 218 (79.6) 223 (81.4) 140 (51.1) 2 (0.7) 2 (0.7)</td>
<td>221 (80.7)</td>
</tr>
</tbody>
</table>

MDR - Multidrug resistant, Amp - Ampicillin, Chl- Chloramphenicol, Tet - Tetracycline, Cot - Cotrimoxazole, Nal - Nalidixic acid, Cip - Ciprofloxacin, OfI - Ofloxacin