

Mycoplasma Anti-Microbial Resistance Patterns In Yaounde Cameroon

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Abstract

Antimicrobial resistance (AMR) is one of the greatest concerns in medical care worldwide and threatens to reverse most of the gains modern medicine brought with the discovery of antimicrobials. Majority of patients received in Etoug-ebe Baptist Hospital Yaounde (EBHY) are treated with antimicrobials. Successful treatment of genital mycoplasma infection remains a priority in a city like Yaounde where prevalence amongst women stands at 65% and has been implicated in pelvic inflammatory disease, puerperal infection, septic abortions, low birth weight, nongonococcal urethritis and prostatitis as well as spontaneous abortion and infertility in women. The aim of the study was to obtain antimicrobial resistance patterns for mycoplasma amongst patients in EBHY. The objectives were to obtain the growth yield rate from microbial culture and sensitivity (MCS) samples in EBHY and to obtain MCS rates in patients served in EBHY, and identify resistance/sensitivity patterns of mycoplasma in EBHY.

The study was a cross-sectional uni-centre retrospective review of MCS results recorded in EBHY in 2016. The recorded data for that year was extracted, tallied, collated and analyzed. The study revealed that mycoplasma organisms showed a mean of 50% resistance (range 24-80%) to some drugs reviewed. There was considerable resistance to tetracycline, tobramycin and to a lower extent azithromycin and ciprofloxacin. Also, of 103 samples cultured for mycoplasma, 30 (29.12%) did not yield any growth. We can conclude that there is a high resistance of mycoplasma to common antibiotics used in EBHY and client treatment should follow resistant pattern guidelines outlined in this research for a successful antimicrobial treatment outcome

1. INTRODUCTION

Antimicrobial resistance has the potential to affect people at any stage of life, as well as the healthcare, veterinary, and agriculture industries. This makes it one of the world's most urgent public health problems (1). Drug resistance in humans has been made worse by the high prevalence of self-medication with antibiotics which often is not properly administered. Self-medication rates in various regions of the world are estimated as follows: South Europe (19%), northern Europe (3%) and central Europe (6%) while in some countries of Africa, close to 100% of antimicrobial use is without prescription and in Asia, it reaches 58% (2). There is a reported 46% increase in the global volume of antibiotic consumption between 2000 and 2018 (3). The high prevalence of antibiotic use and high prevalence of self-medication in low and middle-income countries like Cameroon provide fertile grounds for antimicrobial resistance to infectious disease treatments. In the field of gynecology sexually transmitted infections remain a major cause of morbidity and effective treatment of such infections requires proper use of antibiotics. In this study, our focus was directed at the resistant patterns of mycoplasma. This is because another study in Yaounde Cameroon revealed a high prevalence of genital mycoplasma of up to 65% (4). This is because another study in Yaounde Cameroon revealed a high prevalence of genital mycoplasma of up to 65% (4). Research has implicated genital mycoplasma in many infections of the female and male genital tracts these include pelvic inflammatory disease, prostatitis and others (4). Infections with mycoplasma which is the smallest living organisms' (size 150-250nm) is challenging to treatment as these organisms do not have a cell wall and hence are by nature resistant to most antibiotics that act on the cell wall (4,5). Resistance to antibiotherapy in this organism is becoming a major public health challenge hence in this study we looked at the drug resistance patterns to mycoplasma hominis and ureaplasma urealyticum in EBHY. An earlier study in Cameroon also showed significant resistance of these organisms to common antibiotics as the study revealed that

Pristinamycin was the most effective antibiotic (92%) and sulfamethoxazole the most resisted (8%) antibiotic by genital mycoplasmas. It was concluded that genital mycoplasma is a problem in Cameroon (4). However, there was paucity of information on the resistant patterns of mycoplasma in Cameroon and in EBHY where about 6000 patients are served each month with antibiotics such information does not exist to guide treatment options, hence the need for this study.

2. MATERIALS AND METHOD

Research Design

The study was a cross-sectional uni-centre retrospective review of mycoplasma MCS results obtained in EBHY in 2016 (Jan 1st to December 31st 2016).

Research population/Sampling procedure

The MCS register in EBHY laboratory was accessed. The recorded MCS results from January 1st to December 31st 2016 were accessed and data was collected with permission from the Cameroon Baptist Convention Health Services (CBCHS) institutional review board (IRB). Patients were kept anonymous with no personal information collected. The patients attending EBHY in 2016 who did mycoplasma MCS tests constituted the research population.

Sample size

All patients who came for mycoplasma MCS in 2016 were included in the study without bias.

Data Analysis

The data was extracted, tallied, collated and analyzed. Tables, bar charts and Microsoft Excel were used to prepare and analyze the data. The total number of cultures was expressed as a ratio of the total clients served and also as a ratio of clients treated with antimicrobials: (number of cultures in 2016/number of clients served in

2016*100) and (number of cultures in 2016/number of clients treated with antimicrobials in 2016*100)

To get the resistance ratio for each antibiotic disc, the number of resistant cases was expressed as a ratio of the total number of clients that yielded this germ; a similar approach was used to calculate sensitivity/intermediate sensitivity ratios. Growth yield ratio was computed by dividing the number of positive yield by the number of MCS carried out (number yielded/number of cultures* 100).

Materials

MYCOFAST and **Mycoplasma IES** were used to culture and do drug sensitivity. Both kits had a similar principle of operation. This kit grows the microbes and then does the antibiotic sensitivity if there is a positive yield.

Ethical consideration

Given that this was a retrospective study, the CBCHS institutional review board gave permission for data collection from the EBHY laboratory.

3. RESULTS

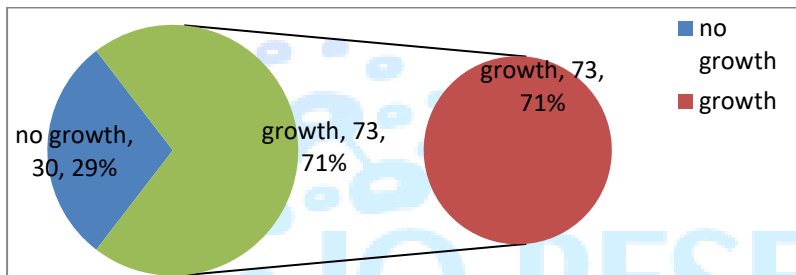


Figure 3.1

103 mycoplasma cultures were carried out. Mycoplasma samples yielding growth rate was 71% (73 samples) while 29% (30 samples) did not yield any growth. 49 of the 73 (67.12%) that grew were cultured for both *Mycoplasma hominis* (Mh) and *Ureaplasma urealyticum* (Uu) ; 19 (26.02%) yielded Uu only and 5 (6.84%) yielded Mh.

3.1: For Mycoplasma Resistance

- 12 Uu & Mh samples out of 49 (24.48%) showed resistance to Ciprofloxacin
- 18 samples Uu & Mh out of 49 (37.23%) showed resistance to Azithromycin
- 23 Uu & Mh samples out of 49 (46.9%) showed resistance to Doxycycline
- 35 Uu & Mh samples out of 49 (71.42%) showed resistance to Tobramycin

6 Uu samples out of 19 (31.57%) showed resistance to doxycycline

4 Mh samples out of 5 (80%) showed resistance to Azithromycin

13 Uu samples out of 19 (68.42%) showed resistance to Ciprofloxacin

3.2: Mycoplasma Intermediate Sensitivity

- 13 samples Uu & Mh out of 49 (26.53%) showed intermediate sensitivity to Josamycin
- 19 samples Uu & Mh out of 49 (38.78%) showed intermediate sensitivity to Azithromycin
- 20 samples Uu & Mh out of 49 (40.81%) showed intermediate sensitivity to Ofloxacin
- 12 samples Uu out of 19 (63.15%) showed intermediate sensitivity to Azithromycin

- 10 samples Uu out of 19 (52.63%) showed intermediate sensitivity to Ofloxacin
- 6 samples Uu out of 19 (31.58%) showed intermediate sensitivity to Norfloxacin
- Only 1 sample Uu out of 19 (5.26%) showed intermediate sensitivity to Ciprofloxacin
- 3 samples Mh out of 5 (60.00%) showed intermediate sensitivity to Ciprofloxacin

3.3: Mycoplasma Full Sensitivity

Uu

- 6 samples out of 19 (31.57%) were sensitive to Doxycycline
- 8 samples out of 19 (42.1%) were sensitive to Tetracycline
- 9 samples out of 19 (47.37%) were sensitive to Pristinamycin
- 6 samples out of 19 (31.57%) were sensitive to Josamycin

Mh

- 5 samples out of 5 (100%) were sensitive to Pristinamycin
- 4 samples out of 5 (80%) were sensitive to Josamycin

Uu & Mh

- 7 samples out of 49 (14.29%) were sensitive to Doxycycline
- 13 samples out of 49 (26.53%) were sensitive to Pristinamycin
- 9 samples out of 49 (18.37%) were sensitive to Josamycin
- 4 samples out of 49 (8.16%) were sensitive to Azithromycin

3.4: Discussion

In this study, up to 29% of samples cultured for mycoplasma did not yield any microbe. This could be associated with poor collection techniques as there were no laboratory records of pre-collection protocols which makes false negative results likely. In females, using lubricants, douches, and disinfectants can affect results; so can monthly menstrual period. In males, urinating within an

hour before testing may affect the results (10). For the 71% of samples that yielded microbes, we confirm 49/73 (67.12%) the presence of co-infection with Mh and Uu which could be associated with the fact that both organisms survive better in alkaline environment (4). This is consistent with findings in Yaounde university teaching hospital where co-infection rates were estimated 20% (4). However, our study reported a higher infection rate than that presented in the study at Yaounde university teaching hospital (4). There were also cases of isolated infections with Mh and Uu. The antibiotics that were commonly used in our setting included: ciprofloxacin, ofloxacin, norfloxacin, azithromycin, doxycycline, tobramycin, josamycin, tetracycline and Pristinamycin. These antibiotics were similar to those used in another study in the Yaounde university teaching hospital by Nunda et al (4) and another study on the gender prevalence and sensitivity of urogenital mycoplasmas to antibiotics in Yaounde, Cameroon (11). This confirms that these are the common antibiotics used in our environment.

Mycoplasmas are normally susceptible to antibiotics that inhibit protein synthesis; for example tetracyclines, macrolides, aminoglycosides, and chloramphenicol, and to fluoroquinolones that inhibit topoisomerases (12) (13) (14) but are resistant to beta-lactam antibiotics, including penicillins and cephalosporins, because they lack a cell wall (15) (16). On the contrary, this study just like others has shown increasing resistance to these antibiotics which were thought to be effective against mycoplasma. For example, a significant resistance rate to ciprofloxacin, ofloxacin, azithromycin and erythromycin was reported, while lower levels were detected for clarithromycin, josamycin and doxycycline (17) (18) (19) consistent with our findings. Also in China, resistance to four of the quinolone antibiotics (i.e., sparfloxacin, levofloxacin, ciprofloxacin, and ofloxacin) and one of the macrolide antibiotics (i.e. acetylspiramycin) was reported and our findings have also suggested increasing resistance to the quinolones. Co-infections showed higher levels of resistance to

these common antibiotics in our study and this was also consistent with reports which indicated that bacteria isolated from coinfections (*U. urealyticum* and *M. hominis*) were completely (100%) resistant to the 14 antibiotics. It also reports high resistance to erythromycin and tetracycline (both 97% resistant) in mixed isolates (*Ureaplasma* species and *M. hominis*) (20). Our study revealed that, with coinfections, the highest rates of sensitivity were seen with Pristinamycin with sensitivity rates of 26.53% followed by azithromycin at 23.99%, josamycin at 18.37%, and doxycycline at 14.29% and the least sensitive was ciprofloxacin with 10.26%. This study also observed decreased rates of sensitivity to common antibiotics in cases of co-infection with both mycoplasma species and these findings were similar to those presented by Ahouga et al in Yaounde (11). While for such co-infections resistance was mostly seen with Tobramycin at 71.4%, doxycycline at 46.9%, azithromycin at 37.23% and ciprofloxacin at 24.48%. We also noted that the quinolones (ciprofloxacin, ofloxacin, norfloxacin) had the highest level of intermediate sensitivity with co-infections. We also noted that for cases of isolated *Uu* infections, Pristinamycin was most sensitive at 47.37% while josamycin and doxycycline had sensitivity rates of 31.57% while ciprofloxacin was least sensitive at 26.38% and most resisted at 68.47%. Hence Pristinamycin and josamycin were most effective against isolated *Uu* infections consistent with findings by Ahouga et al in Yaounde (11). On the other hand, isolated infections with *Mh* was 100% sensitive to Pristinamycin, 80% sensitive to josamycin consistent with findings by Ahouga et al in Yaounde (11), it was 100% resistant to azithromycin and over 60% resistant to all quinolones and this was also consistent with findings in other studies in Yaounde (11). There is a growing resistance to the tetracycline and macrolides which were initially the drugs of choice for the treatment of mycoplasma infections.

CONCLUSION

From the sensitivity pattern for mycoplasma displayed in this study, there is evidence to

confirm that these organisms are developing resistance to common antibiotics used in our environment and a more careful approach to the choice of antibiotics for empirical treatment is needed. While pristinamycin, josamycin, and azithromycin remain sensitive in most cases, they are less commonly available for use and the readily available quinolones and doxycycline are showing increasing resistance.

RECOMMENDATIONS

1. Mycoplasma samples showed significant resistance to Ciprofloxacin, Doxycycline, Azithromycin, Tobramycin, in decreasing order but the germ is sensitive to Josamycin, Ofloxacin, Pristinamycin. It is advisable from these results to do MCS to determine the best antibiotic to use especially in patients whose treatment seems not to be responding to mainstream antibiotics.
2. Josamycin, Ofloxacin, Pristinamycin may be considered in the empirical treatment of Mycoplasma infections
3. Josamycin showed good activity in most mycoplasma samples and is worth considering for addition in to the EBHY formulary replacing Azithromycin.
4. There is considerable resistance to Tetracycline, Tobramycin and to a lesser extent Azithromycin. These drugs should no longer be the first line in managing mycoplasma infections.

Suggestion for Further Research

The results of this study give reason for us to consider carrying out similar studies in other institutions of the CBCHS in other towns of Cameroon. These studies should be better planned prospective controlled trials so the results are more useful. Such results can then be meta-analyzed and more scientifically based decisions taken on the management of patients.

ACRONYMS

AMR.....	Antimicrobial resistance
MCS.....	Microbial Culture and Sensitivity
WHO.....	World Health Organization
Uu.....	Ureaplasma urealyticum
Mh... ..	Mycoplasma hominis
CBCHS.....	Cameroon Baptist Convention Health services
EBHY.....	Etoug-Ebe Baptist Hospital Yaoundé
STI.....	sexually transmitted infection
PCR	polymerase chain reaction
<u>CDC</u>	<u>Centers for Disease Control and Prevention</u>
IRB.....	Institutional Review board

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