RUSSIAN MULTICENTER EXTERNAL QUALITY CONTROL ASSESSMENT (EQA) OF ANTIMICROBIAL SUSCEPTIBILITY TESTING (AST) IN 2002: HIGHLIGHTS OF THE PROBLEMS

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ABSTRACT

Background: Quality assessment (QA) in clinical microbiology is of extreme value to ensure reliability of pathogens' identification and AST results.

Objective: To evaluate reliability of identification and AST data generated by microbiological laboratories in geographically distinct regions of Russia.

Methods: Five quality control strains (MRSA; susceptible *E. coli*; ESBL-producing *E. coli*; Pen-R *S. pneumoniae;* VR-*E. faecium* with HLAGR;) selected by European Antimicrobial Resistance Surveillance System (EARSS) and provided by Pasteur Insititute (Paris, France) and National External Quality Assessment Scheme (NEQAS) (London, UK) were distributed by IACMAC to 45 laboratories in 24 cities in Russia. Rates of minor, major and very major errors in AST results *vs* referent NEQAS data were calculated (FDA, USA, 2003).

Results: There were no significant problems with identification of all bacterial isolates, but *E. faecium*. It was correctly identified to the species level in 63% and to the genus level in 96%. AST of susceptible *E. coli* isolate raised no noticeable problems. However resistance mechanisms detedction in MRSA, ESBL-producing *E. coli*, Pen-R *S. pneumoniae* and Van-R/HLAGR *E. faecium* was poor, leading to high rates of very major errors as follows: 36% (16/44); 6-10-72% (2/31-4/39-28/39) for ceftriaxone-cefotaxime-ceftazidime; 3% (1/40) for oxacillin, 28% (10/36) for penicillin; 19% (8/42) and 10% (4/40), respectively for these resistances in the above bacteria.

Conclusions: 1) majority of laboratories are unable to detect clinically important resistance mechanisms (MRSA, ESBLs, Pen-R in pneumococci and Van-R/HLAGR in enterococci), 2) these data dictate the necessity to perform multicentre surveillance studies with AST in the reference center.

INTRODUCTION

The impact of AST on effective antibacterial therapy is of increasing importance due to emergence and spread of antimicrobial resistance in bacteria. The results of AST *in vitro* serve as basis for administration of optimal antibiotic regimen for current patient, for empirical choice of antimicrobials and for creating of hospital formulary.

Strict standardization of the testing procedure and regular performing of quality control tests are essential for achieving of repeatable clinically relevant results. External quality assessment (EQA) in clinical microbiology is of extreme value to ensure reliability of pathogens' identification and AST results.

The objective of the current study was to evaluate reliability of identification and AST with emphasis to detection of clinically significant resistance mechanisms in microbiological laboratories of geographically distinct regions of Russia.

METHODS

Five quality control strains listed in Table 1 (MRSA; susceptible *E. coli*; ESBL-producing *E. coli*; Pen-R *S.pneumoniae;* VR-E. *faecium* with HLAGR) selected by European Antimicrobial Resistance Surveillance System (EARSS) and provided by Pasteur *Insititute* (Paris, France) and National External Quality Assessment Scheme (NEQAS) (London, UK) were distributed by Inter-Regional Association for Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC, Russia) to 45 laboratories in 24 Russian cities.

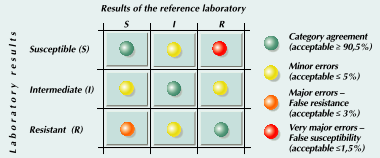
Table 1. Characteristics of the EQA strains

U2A 1556	*S. aureus*	MRSA, mecA, pen A, ant4'
U2A 1557	*E. coli*	IRT
U2A 1526	*E. coli*	blaCTX-M, aac3-V, ant3", gyrA
U2A 1580	*S. pneumoniae*	penR, aph3'-III, ant3"9, ermB, parC, cat, TpRSuR
U2A 805	*E. faecium*	vanB, aph2"-aac6'ant3"9, erm

Fig. 1. Participating centers

Rates of minor, major and very major errors in AST results *vs* referent NEQAS data were calculated according to FDA (Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, 2003). For data analysis conventional acceptable rates of discrepancies were utilized (Figure 2).

Fig. 2. Definitions of discrepancies in AST results of participating laboratories and UK NEQAS reference data



RESULTS

Results of identification of EQA strains by participating laboratories are presented in the Table 2.

Table 2. Results of EQA strains identification by participating laboratories

Strain		Results of Identification (*n* of laboratories / %)		
		Correct to the species level	Correct to the genus level	Incorrect
U2A 1556	*S. aureus*	45/45 / 100%	45/45 / 100%	0
U2A 1557	*E. coli*	38/45 / 84%	44/45 / 98%	1/45 / 2%
U2A 1526	*E. coli*	40/45 / 89%	45/45 / 100%	0
U2A 1580	*S. pneumoniae*	43/44 / 98%	44/44 / 100%	0
U2A 805	*E. faecium*	29/45 / 63%	43/45 / 96%	2/45 / 4%

The results revealed no significant problems with identification of all bacterial isolates, but *E. faecium*. It was correctly identified to the species level in 63% and to the genus level in 96%.

AST of EQA strains in the participating laboratories was performed using different methods, testing media and interpretive criteria («Methodical Rules» by Ministry of Health of USSR (1983), NCCLS guidelines (various editions) and AST device manufacturers' recommendations). The results of AST of EQA strains are presented in Tables 3-7.

Table 3. AST Results of S.aureus U2A 1556 (MRSA, mecA «+»)

Antimicrobial	*n* (%) of labs reporting result as		
	S	I	R
Vancomycin	42(98)	1(2)	0(0)
Gentamicin	41(92)	2(4)	0(0)
Oxacillin	16(36)	1(2)	27(62)
Rifampin	2(5)	0(0,0)	38(95)
Tetracycline	41(93)	3(7)	0(0)

Table 4. AST Results of E. coli U2A 1557 (IRT)

Antimicrobial	*n* (%) of labs reporting result as		
	S	I	R
Ampicillin	0(0,0)	6(15)	33(85)
Ceftriaxone	29(97)	0(0)	1(3)
Ceftazidime	39(98)	0(0)	1(2)
Cefotaxime	41(95)	2(5)	0(0)
Gentamicin	41(92)	2(4)	2(4)
Amikacin	38(89)	1(2)	4(9)
Ciprofloxacin	40(93)	3(7)	0(0)

Table 5. AST Results of E.coli U2A 1526 (ESBL +)

Antimicrobial	*n* (%) of labs reporting result as		
	S	I	R
Ampicilin	0(0)	0(0,0)	39(100)
Ceftriaxone	2(6)	6(19)	23(74)
Cefotaxime	4(10)	11(28)	8(20)
Ceftazidime	28(72)	3(8)	8(20)
Gentamicin	3(7)	0(0)	41(93)
Amikacin	1(2)	0(0)	24(62)
Ciprofloxacin	43(96)	2(4)	0(0)

Table 6. AST Results of S. pneumoniae U2A 1580 (Pen-R)

Antimicrobial	*n* (%) of labs reporting result as		
	S	I	R
Oxacillin	1(3)	2(5)	37(92)
Penicillin G	10(28)	10(28)	16(44)
Ceftriaxone	27(84)	5(16)	0(0)
Cefotaxime	18(86)	2(10)	1(4)
Ciprofloxacin	29(82)	4(14)	1(4)
Erythromycin	2(6)	0(0)	33(94)
Clindamycin	5(14)	1(3)	29(83)

Table 7. AST Results of E.faecium U2A 805

Antimicrobial	*n* (%) of labs reporting result as		
	S	I	R
Ampicillin	0(0)	0(0)	14(100)
Amoxicillin	0(0)	0(0)	41(100)
Vancomycin	8(19)	10(24)	24(57)
High level gentamicin resistance	4(10)	0(0)	36(90)

DISCUSSION

The obtained results of EQA strains testing presume that AST of clinical isolates in routine practice in Russian microbiology laboratories produce a lot of errors.

Some sources of the false results revealed when analyzing laboratories' reports for the EQA exercise are as follows:

1. *S. aureus*
   - Use of 5 or 10 μg oxacillin disks (instead of recommended 1 μg) for AST in 5/36 (14%) of laboratories
2. ESBL-producing *E.coli*
   - Unavailability of ESBLs detection method in routine laboratory practice in 12/45 (26%) of laboratories
   - Failure to detect ESBLs production in 3/29 (10%) of laboratories having some method of ESBLs detection
   - Incorrect interpretation of the AST results of 3rd gen. cephalosporins (ceftriaxone, cefotaxime and ceftazidim) in ESBL-positive strains
3. *S. pneumoniae*
   - Screening for penicillin resistance with 5 or 10 μg oxacillin disks (instead of recommended 1 μg) in 5/33 (15%) of laboratories
   - Testing of penicillin and cephalosporins (ceftriaxone, cefotaxime) susceptibility by disk diffusion method, that leads to unreliable results in 72% (26/36), 75% (24/32) and 86% (18/21) of participating laboratories, respectively.
4. *Enterococcus spp.*
   - Lack of knowledge of HLAGR (gentamicin) detection method and use of 10 μg gentamicin disk instead of 120 μg in 9/40 (22,%) laboratories.
   - Errors in detection of HLAGR (gentamicin) in 4/25 (16%) laboratories using 120 μg gentamicin disk.
   - Errors in detection of vancomycin resistance in 18/43 (43%) laboratories.

Thus, the above results elucidate significant problems with personnel proficiency, AST procedures standardization and internal quality control in most of the Russian laboratories. There is a vast need for task-oriented educational activities and creation of National guidelines for AST and detection of clinically significant antimicrobial resistance mechanisms (MRSS, ESBLs, HLAGR, etc.) in Russia, harmonized with international practices (WHO, NCCLS, EUCAST, etc.).

CONCLUSION

1. Majority of laboratories are unable to detect clinically important resistance mechanisms (MRSA, ESBLs, Pen-R in pneumococci and Van-R/HLAGR in enterococci),
2. Based on obtained data, the most rational approach currently is the performance of multicentre antimicrobial surveillance studies with the testing in selected reference laboratory.

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