Inducible clindamycin resistance in clinical isolates of Staphylococcus aureus due to erm genes, Iran

Mojtaba Moosavian1,2; Saeed Shoja3; Soodabeh Rostami4*; Maryam Torabipour2; Zahra Farshadzadeh5

1Department of Microbiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. 2Health Research Institute, Infectious and Tropical Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. 3Infectious and Tropical Diseases Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. 4Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. 5Department of Microbiology, Tehran University of Medical Sciences, Tehran, Iran.

ABSTRACT

Background and Objectives: Resistance to macrolide can be mediated by erm and msrA genes in Staphylococcus aureus. There are the evidences that show erm genes may be causative agent of inducible or constitutive resistance. The aim of this study was to investigate the incidence of inducible clindamycin resistance and determine the most frequency of erm and msrA genes among S. aureus isolates.

Materials and Methods: In this study a total of 124 non duplicated clinical isolates of S. aureus were tested with disk diffusion method. All isolates were tested by PCR for meca, ermA, ermB, ermC and msrA genes.

Results: According to PCR results, 48.4% had meca gene and 51.6% were meca negative. By phenotypic D-test method, 32.3% revealed inducible resistance and recorded as D and D+. Sensitive and constitutive phenotypes were found in 54.8% and 12.9% of isolates respectively. Inducible clindamycin resistance was more prevalent in MRSA (29%) than MSSA isolates (2.4%). Among studied erm genes, the most frequency genes were ermA and ermC with 41.1% and 17.7% respectively. Three isolates of them had D phenotype, while the PCR results of erm genes were negative. All isolates were negative for ermB or msrA genes.

Conclusion: Since S. aureus isolates with inducible resistance may mutate and change to constitutive resistance, to prevent treatment failure, we suggest that inducible resistance test be performed on erythromycin resistant/clindamycin sensitive isolates.

Keywords: D- test, Inducible clindamycin resistance, Staphylococcus aureus

INTRODUCTION

In the past decade Staphylococcus aureus especially methicillin-resistant strains were known as the most important pathogens that were frequently isolated, and caused serious and life threatening clinical infections such as nosocomial and community-acquired infections (1-3). Vancomycin and teicoplanin are commonly used to treat the infections with methicillin-resistant S. aureus (MRSA)(1), however, recently isolation of S. aureus with decrease susceptibility or resistance to glycopeptides (4) caused encourage of physicians to prescribe of other alternative treatments such as Macrolide - Lincosamide - Streptogramin (MLS) (5).
Macrolide (erythromycin), lincosamide (clindamycin), and streptogramin (quinupristin-dalfopristin) antimicrobial agents (collectively MLS agents) have been used to treat staphylococcal infections (6).

However, among MLS because of pharmacokinetics properties such as good oral absorption and excellent tissue penetration, clindamycin is the most used antibiotic, but excessive use of MLS in the treatment of infections, has been led to increase of resistance to these antibiotics (5). Resistance to MLS antibiotics among staphylococci can be occurred by various mechanisms, including: I- an active efflux pump encoded by msrA gene (cause resistance to macrolids and type B streptogramins, and not to clindamycin) (6), II- Enzymatic inactivation of antibiotic (7) and III- ribosomal target modification that is the major mechanism of resistance (8) and affects macrolides, lincosamides, and type B streptogramins (MLS$_b$ resistance)(6, 9). In staphylococci, the four genes,ermA, ermB, ermC and ermF are frequently involved in resistance to MLS (10). The expression of MLS$_b$ resistance can be inducible or constitutive and is not related to the type of the erm genes (8). S. aureus isolates with constitutive resistance in vitro, demonstrate resistance to both erythromycin and clindamycin whereas S. aureus isolates that harbor inducible resistance are resistant to erythromycin but appear susceptible to clindamycin (iMLS$_b$) (11). Although, after contact to clindamycin in vivo, they may mutate and produce constitutive resistance that becoming resistant to all MLS antibiotics (12) and may cause treatment failure (13-14). In addition, isolates with msrA-mediated efflux pump also have the same phenotype and are resistant to erythromycin and sensitive to clindamycin, however they cannot produce constitutive resistance during treatment (14).

Lack of identity of inducible clindamycin resistance leads to false laboratory reports and could lead to clinical failure when clindamycin is used therapeutically and cause treatment problems (6, 15). On the other hand, labeling of staphylococci as clindamycin resistant, while they are only resistance to erythromycin, could stop prescription of clindamycin, in cases that infections have occurred by truly clindamycin-susceptible staphylococcal isolates (6, 16). A simple laboratory test (as titled D-zone test) can differentiate between staphylococci that have inducible erm genes-mediated resistance and those which have efflux pump-mediated resistance (14).

The aim of present study was to determine the incidence of inducible clindamycin resistance and investigate the prevalence of ermA, ermB, ermC, and msrA genes among the clinical isolates of S. aureus.

**MATERIALS AND METHODS**

**Isolation and identification of bacteria.** During of one year period 124 clinical isolates of S. aureus were collected from three teaching hospitals affiliated to Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. The bacteria which were consecutively isolated from patients in various wards and different specimens such as: catheter, blood, wound, discharge, abscess, burn, and so on, were transported to Microbiology Laboratory in School of Medicine and were confirmed by standard microbiology tests including: Gram staining, catalase, slide and tube coagulase, mannitol fermentation and production of DNase enzyme (17).

**Antibiotic susceptibility testing.** Antimicrobial susceptibility of the isolates was determined by using Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standard Institute (CLSI) guidelines. Briefly a 0.5 McFarland suspension of bacteria were prepared and inoculated on Mueller-Hinton’s agar plates (Merck, Germany). The tested antimicrobial agents were penicillin (10U), oxacillin (1µg), cefoxitin (30µg), gentamicin (10µg), Trimetoprim-sulfametoxazol (1.25/23.75µg), azithromycin (15µg), imipenem (10µg), meropenem (10µg), ciprofloxacin (5µg) and rifampin (5µg). The minimal inhibitory concentrations (MICs) of vancomycin were determined by E-Test (Bio Mérieux) according to CLSI guidelines. S. aureus ATCC 25923 and S. aureus ATCC 29213 were included as standard strains and quality control for disk diffusion and MIC tests; respectively (CLSI, 2007).

**Disk approximation test with erythromycin and clindamycin (D-Zone test).** Inducible clindamycin resistance, was determined using disk approximation test with erythromycin and clindamycin (D-zone test) as recommended by CLSI (CLSI, 2007). Briefly, 0.5 McFarland suspensions were prepared with organisms from an overnight growth and then inoculated and spread over the surface on Mueller-Hinton’s agar plates (Merck, Germany). One erythromycin disk (15 µg) and one clindamycin disk (2 µg) (MAST, Group Ltd, Merseyside, UK) were
placed on the inoculated plates in a distance of 15 mm from each other. Plates were incubated at 35°C and read after 18 h. Inducible clindamycin resistance was confirmed by forming of a flattening shape of the clindamycin inhibition zone (D shape) around the erythromycin disk which indicated erythromycin had induced clindamycin resistance. Furthermore, the staphylococcal isolates were grouped to different phenotypes according to a study as previously described (14). These phenotypes were: S phenotype (sensitive to both erythromycin and clindamycin), R phenotype (constitutive resistance and were resistant to both erythromycin and clindamycin), D phenotype (resistant to erythromycin and clindamycin zone like D) and D+ (resistant to erythromycin and D shape zone for clindamycin with small colonies growing around the erythromycin disk (14).

**DNA extraction.** DNA was extracted from *S. aureus* isolates by boiling method (2). Bacteria were inoculated on Mueller-Hinton’s agar plate overnight at 37°C. After this time, one to five colonies were inoculated on Mueller-Hinton’s agar plate overnight and used as DNA template for PCR reaction (2).

**Identification of mecA gene.** For identification of mecA gene in methicillin-resistant isolates, which were screened by resistance to oxacillin and/or cefoxitin disks, polymerase chain reaction (PCR) was performed using by primer pair mecA F 5’-GTGAAAATGCTACTGAGCCTCAGTGA-3’ and mecA R 5’-CCAATTCACATGTGTTGCTCTAA-3’, that amplified a 310-bp Product (Tiwari and Sen, 2006). PCR condition in a Mastercycler (Eppendorf, Germany) were as follows: Initial denaturation, 95°C for 3 min; 35 cycles of 95°C for 30 s, various annealing temperatures (58°C for ermC, 62.8°C for ermB, 59°C for ermA, 55°C for msrA) for 30 s and 72°C for 45 s and final extension at 72°C for 7min. PCR products were analyzed by separating on 1.5% agarose gel electrophoresis, then were stained with ethidium bromide solution and finally visualized in gel documentation system (10). One *S. aureus* isolate with ermA and another one with ermC were sequenced and used as positive control for identification of these genes. We also used another native isolate as positive control for msrA gene. Furthermore, a reaction containing all materials except DNA was used as negative control. Distilled water was used instead of DNA in negative control reaction.

**Statistical analyses.** The results were analyzed using the SPSS for windows software version 19. Fisher’s exact test or chi-square, as appropriate, was used to compare frequencies. *P*-value of ≤ 0.017 was considered as statistically significant.

**RESULTS**

In this study a total of 124 *S. aureus* isolates, which were collected from different hospital wards were examined. The frequencies of *S. aureus* isolated from different clinical samples are shown in Table 1. The results of antimicrobial sensitivity test showed that all isolates were susceptible to vancomycin (100% susceptible) and the majority of them were resistant to penicillin (96.8%). The results of antibiotic
susceptibility testing for other antibiotics are shown in the Table 2.

As mentioned above, the results of vancomycin E-test showed that all of staphylococcal isolates were sensitive to vancomycin and their MIC to this antibiotic was in range 0.5µg/ml to 2µg/ml, with MIC 50 = 1µg/ml and MIC 90 = 1.5µg/ml. Based on the results of D-Zone test, different phenotypes of *S. aureus* including S phenotype (54.8%), R phenotype (12.9%), D phenotype (31.5%) and D + (0.8%) were observed (Fig. 1). The prevalence of different phenotype among each specimen is shown in Table 1.

The electrophoresis results of PCR products showed that 48.4% and 51.6% of isolates were positive and negative for *mecA* gene, respectively. The rate of inducible clindamycin resistance in methicillin-resistant isolates was higher than in MSSA isolates (*P*-value< 0.001). The rate of D, D’, S and R phenotypes among MRSA isolates were 29%, 0%, 6.5% and 12.9% respectively. Among MSSA isolates 2.4%, 0.8%, 48.4% and 0% had D, D’, S and R phenotypes respectively. According to PCR results, 41.1% isolates had *ermA* (Fig. 2) but 17.7% contained *ermC* (Fig. 3). Twenty isolates (16.1%) were

### Table 1. Frequency of *S. aureus* isolates in various clinical specimens and different phenotypes

| Specimen      | D (%) | D’ (%) | S (%) | R (%) | Negative (%) | Number (%) |
|---------------|-------|--------|-------|-------|--------------|------------|
| Burn          | 17.7  | 0      | 7.3   | 1.6   | 0            | 33 (26.6)  |
| Wound         | 4.8   | 0      | 16.1  | 4     | 0            | 31 (25)    |
| Blood culture | 3.2   | 0      | 8.1   | 2.4   | 0            | 17 (13.7)  |
| Catheter      | 4     | 0      | 7.3   | 0.8   | 0            | 15 (12.1)  |
| Discharge     | 0     | 4.8    | 6.5   | 1.6   | 0            | 10 (8.1)   |
| Trachea       | 0.8   | 0      | 3.2   | 0.8   | 0            | 6 (4.8)    |
| Urine culture | 0     | 4.8    | 2.4   | 0     | 0            | 3 (2.4)    |
| Corneal lesion| 0     | 0      | 1.6   | 0.8   | 0            | 3 (2.4)    |
| Abscess       | 0     | 0      | 0.8   | 0.8   | 0            | 2 (1.6)    |
| Nasal swab    | 0     | 0      | 0.8   | 0     | 0            | 2 (1.6)    |
| Nail infection| 0     | 0      | 0     | 0     | 0            | 1 (0.8)    |
| Pleural effusion| 0  | 0      | 0.8   | 0     | 0            | 1 (0.8)    |
| Total         | 31.5  | 0.8    | 54.8  | 12.9  | 0            | 124 (100)  |

D: Resistant to erythromycin and clindamycin zone like D, D’ : Resistant to erythromycin and D shape zone for clindamycin with small colonies growing within the D zone, S: Sensitive, R: Resistant, Negative: Resistant to erythromycin and susceptible to clindamycin and lack of D shape zone

### Table 2. The results of antibiogram test for *S. aureus* isolates

| Antibiotic                           | Sensitive (%) | Intermediate (%) | Resistant (%) |
|--------------------------------------|---------------|-----------------|--------------|
| Penicillin                           | 4 (3.2)       | -               | 120 (96.8)   |
| Oxacillin                            | 69 (55.6)     | -               | 55 (44.4)    |
| Cefoxitin                            | 64 (51.6)     | -               | 60 (48.4)    |
| Gentamicin                           | 71 (57.3)     | 2 (1.6)         | 51 (41.1)    |
| Trimetoprim-sulfamethoxazole         | 84 (67.7)     | -               | 40 (32.3)    |
| Azithromycin                         | 66 (53.2)     | -               | 58 (46.8)    |
| Vancomycin                           | 124 (100)     | -               | -            |
| Imipenem                             | 103 (83.1)    | 2 (1.6)         | 19 (15.3)    |
| Meropenem                            | 122 (98.4)    | -               | 2 (1.6)      |
| Ciprofloxacin                        | 68(54.8)      | 3(2.4)          | 53(42.7)     |
| Rifampin                             | 100 (80.6)    | 13 (10.5)       | 11 (8.9)     |
| Clindamycin                          | 66(53.2)      | -               | 58(46.8)     |
| Erythromycin                         | 66(53.2)      | 1(0.8)          | 57(46)       |
positive for both \( \text{erm}A \) and \( \text{erm}C \). Three isolates had D phenotype while the results of \( \text{erm} \) genes PCR were negative. All isolates were negative for \( \text{erm}B \) and \( \text{msr}A \) genes. The result of PCR for \( \text{erm} \) genes according to sensitivity to methicillin is shown in Table 3.

**DISCUSSION**

For microbiology laboratories there is important to correctly recognize and report an \( S. \ aureus \) isolate, which is truly clindamycin susceptible when it’s erythromycin resistant, and clindamycin susceptible. This true result may depend obtained by using a simple disk diffusion, described as D – zone test, because of this test can exclude inducible clindamycin resistance (18). Prevalence of \( S. \ aureus \) isolates with inducible resistance can be depending on geographic region, patient’s age, species of bacteria, sample origin and source of the strains like community or nosocomial. Prevalence of inducible rate is also different from a hospital to another hospital and even among patients (10, 19-20).

The results of our study have shown that incidence of inducible clindamycin resistance was 32.3% among all isolates. Rahbar *et al.* in Iran showed that 10.8% of \( S. \ aureus \) isolates had iMLS \( B \) (21). Jethwani *et al.* in India showed that 43% of \( S. \ aureus \) isolates were iMLS \( B \). Dizbay *et al.*, in Turkey, reported that 90% erythromycin resistant, clindamycin sensitive \( S. \ aureus \) showed inducible clindamycin resistance (23).

As mentioned, the rate of inducible resistance may vary depending on the resistance bacteria to methicillin (21). In our study iMLS \( B \) was most prevalent in MRSA (29%) compared to MSSA (3.2%) isolates (\( P \)-value <0.001). The prevalence of iMLS \( B \) resistance in MRSA has been previously reported as highly variable, from12.3% to 35.9%, in different parts of the world (7, 11, 15, 19, 21, 24-25). Similar to MRSA, the prevalence rate of iMLS \( B \) is variable among MSSA isolates. In present study 3.2% of MSSA had iMLS \( B \) phenotype. This rate has been reported variously from different countries. Some of these reports showed iMLS \( B \) rates from 4% to 68% (7, 11, 15, 19, 21, 25).

Our results showed that S phenotype rate with 48.4% was the most prevalent among MSSA isolates, while, its rate was 6.5% among MRSA (\( P \)-value < 0.001). Similar to D phenotype, the prevalence of S phenotype is very variable among MSSA and MRSA in different countries. The prevalence rate of S phenotype in

http://ijm.tums.ac.ir
Table 3. Results of erm genes PCR according sensitivity to methicillin for the S. aureus isolates

| Genotype | Results | Sensitivity to methicillin |
|----------|---------|---------------------------|
|          |         | MRSA (%) | MSSA (%) |
| ermA     | positive | 39.5      | 1.6      |
|          | negative | 2.4       | 1.6      |
| ermC     | positive | 16.9      | 0.8      |
|          | negative | 25        | 2.4      |
| ermB     | positive | 0         | 0        |
|          | negative | 0         | 0        |
| msrA     | positive | 0         | 0        |
|          | negative | 0         | 0        |

MSSA has been reported 14% to 90.9% and among MRSA isolates from 0% to 26.3% (7, 15, 21-22).

We detected constitutive resistance (12.9%) only in MRSA, but it was not found in MSSA isolates. This type of resistance has been reported from 8 to 64.6% in MRSA and 1.6 to 13% in MSSA isolates in different parts of the world (11, 15, 21-23, 26).

The results of PCR in our study showed that only ermA with 41.1% and ermC with 17.7% were found among studied isolates. No ermB or msrA was detected in this study. Westh et al. in Denmark showed that among S. aureus strains isolated from 1959 to 1988, ermA and ermC were responsible for 98% resistance to erythromycin (27). Cetin et al. in Turkey found that 62% and 17% of S. aureus isolates were positive for ermA & ermC genes respectively (26). Saderi et al. in Tehran reported 60.3% and 54.8% of genes belonged to ermA and ermC respectively in S. aureus strains (28). We have not found any msrA gene, although different rates of msrA genes among S. aureus isolates had been reported (10, 26). Lina et al. showed that msrA was more prevalent in coagulase-negative staphylococci (29). Prevalence of ermB is low and few studies reported this gene in S. aureus. Coutinho et al. reported that between 45 isolates of S. aureus only, 1 isolate had ermB(20), while in Aktas et al. report, this rate was 8.3% (10). Lina et al. showed only one isolate with ermB among 144 isolates of S. aureus (29). Cetin et al. reported the same as present study, found no ermB gene in 47 S. aureus isolates (26). We detected that 16.1% of isolates had both ermA & ermC. Some of the studies also found both ermA and ermC among S. aureus isolates (10, 26).

In our study three S. aureus isolates showed inducible clindamycin resistance (D phenotype), while the results of erm genes PCR were negative. Similar findings have been previously reported. Aktas et al. found that 16.6% of S. aureus isolates were PCR negative (10). Saderi et al. in Tehran studied S. aureus strains for ermA & ermC and reported that 33.3% of strains were negative for both genes (28). Other phenotypes including Hazy D (HD) or Negative (Neg) that previously described (14), were not found in our study. In the present study, all the erythromycin resistant isolates and clindamycin susceptible showed inducible resistance and no negative phenotype was identified among them. In conclusion, we recommend that microbiology laboratories in hospitals perform the D test for any S. aureus isolate that is resistant to erythromycin and sensitive to clindamycin.

ACKNOWLEDGEMENT

This study was jointly funded by Vice-Chancellor for research affairs and Infectious Disease & Tropical Research Center of Ahvaz Jundishapur University of Medical Sciences (Project No. 88114). We appreciate the Center for Developing Clinical Research for the consultation and statistical analysis. Thanks also should be extended to the people of the Research Consultation Center (RCC), for their technical support.

REFERENCES

1. Guerin F, Buu-Hoi A, Mainardi JL, Kac G, Colardelle N, Vaupre S, et al. Outbreak of methicillin-resistant Staphylococcus aureus with reduced susceptibility to glycopeptides in a Parisian hospital. J Clin Microbiol 2000;38:2985-2988.
2. Nunes EL, dos Santos KR, Mondino PJ, Bastos Mdo C, Giambiagi-deMarval M. Detection of ileS-2 gene encoding mupirocin resistance in methicillin-resistant Staphylococcus aureus by multiplex PCR. Diagn Microbiol Infect Dis 1999;34:77-81.
3. Soge OO, Meschke JS, No DB, Roberts MC. Characterization of methicillin-resistant Staphylococcus
aureus and methicillin-resistant coagulase-negative Staphylococcus spp. isolated from US West Coast public marine beaches. J Antimicrob Chemother 2009;64:1148-55.
4. Tiwari HK, Sen MR. Emergence of vancomycin resistant Staphylococcus aureus (VRSA) from a tertiary care hospital from northern part of India. BMC Infect Dis 2006;6:156.
5. Prabhu K, Rao S, Rao V. Inducible clindamycin resistance in Staphylococcus aureus isolated from clinical samples. J Lab Physicians 2011;3:25-27.
6. Zelazny AM, Ferraro MJ, Glennen A, Hindler JF, Mann LM, Munro S, et al. Selection of strains for quality assessment of the disk induction method for detection of inducible clindamycin resistance in Staphylococci: a CLSI collaborative study. J Clin Microbiol 2005;43:2613-2615.
7. Yilmaz G, Aydin K, Iskender S, Caylan R, Koskal I. Detection and prevalence of inducible clindamycin resistance in staphylococci. J Med Microbiol 2007;56(Pt 3):342-345.
8. Wondrack L, Massa M, Yang BV, Sutcliffe J. Clinical strain of Staphylococcus aureus inactivates and causes efflux of macrolides. Antimicrob Agents Chemother 1996;40:992-998.
9. Prunier AL, Malbruny B, Tande D, Picard B, Leclercq R. Clinical isolates of Staphylococcus aureus with ribosomal mutations conferring resistance to macrolides. Antimicrob Agents Chemother 2002;46:3054-6305.
10. Aktas Z, Aridorogan A, Kayacan CB, Aydin D. Resistance to macrolide, lincosamide and streptogramin antibiotics in staphylococci isolated in Istanbul, Turkey. J Microbiol 2007;45:286-290.
11. Gupta V, Datta P, Rani H, Chander J. Inducible clindamycin resistance in Staphylococcus aureus: a study from North India. J Postgrad Med 2009;55:176-179.
12. Navaneeth BV. A preliminary in vitro study on inducible and constitutive clindamycin resistance in Staphylococcus aureus from a South Indian tertiary care hospital. Int J Infect Dis 2006;10:184-185.
13. Siberry GK, Tekle T, Carroll K, Dick J. Failure of clindamycin treatment of methicillin-resistant Staphylococcus aureus expressing inducible clindamycin resistance in vitro. Clin Infect Dis 2003;37:1257-1260.
14. Steward CD, Raney PM, Morrell AK, Williams PP, McDougall LK, Jevitt L, et al. Testing for induction of clindamycin resistance in erythromycin-resistant isolates of Staphylococcus aureus. J Clin Microbiol 2005;43:1716-1721.
15. Chelae S, Laohapretrthisarn V, Phengmak M, Kongmuang U, Kalnawakul S. Detection of inducible clindamycin resistance in staphylococci by disk diffusion induction test. J Med Assoc Thai, 2009 Jul; 92:947-951.
16. Fiebelkorn KR, Crawford SA, McElmeel ML, Jorgensen JH. Practical disk diffusion method for detection of inducible clindamycin resistance in Staphylococcus aureus and coagulase-negative staphylococci. J Clin Microbiol 2003;41:4740-744.
17. Winn W, Allen S, Janda W, Koneman E, Procop G, Schreckenberger P, et al(2006). Gram-Positive Cocci Part I. In: Koneman’s Color Atlas and Textbook of Diagnostic microbiology. Lippincott Williams & Wilkins,6th ed. Philadelphia, USA, pp. 623-671.
18. Fernandes CJ, O’Sullivan MV, Cai Y, Kong F, Zeng X, Gilbert GL, et al. Agar dilution method for detection of inducible clindamycin resistance in Staphylococcus spp. J Clin Microbiol 2007;45:4018-4020.
19. Levin TP, Suh B, Axelrod P, Truant AL, Fekete T. Potential clindamycin resistance in clindamycin-susceptible, erythromycin-resistant Staphylococcus aureus: report of a clinical failure. Antimicrob Agents Chemother 2005;49:1222-1224.
20. Coutinho Vde L, Paiva RM, Reiter KC, de-Paris F, Barth AL, Machado AB. Distribution of erm genes and low prevalence of inducible resistance to clindamycin among staphylococci isolates. Braz J Infect Dis 2010;14:564-568.
21. Rahbar M, Hajia M. Inducible clindamycin resistance in Staphylococcus aureus: a cross-sectional report. Pak J Biol Sci 2007;10:189-192.
22. Jethwani UN MSA, Shah Latika N. Detection of inducible clindamycin resistance by an automated system in a tertiary care hospital. Afr J Microbiol Res 2011;5:3.
23. Dizbay M, Gunal O, Ozkan Y, Ozcan Kanat D, Altunecik A, Arman D. Constitutive and inducible clindamycin resistance among nosocomially acquired staphylococci. Mikrobiyol Bul 2008;42:217-221.
24. Tashakori M, Mohseni Moghadam F, Ziasheikholeslami N, Jafarpour P, Bahsoun M, Hadavi M, et al. Staphylococcus aureus nasal carriage and patterns of antibiotic resistance in bacterial isolates from patients and staff in a dialysis center of southeast Iran. Iran J Microbiol 2014;6:5.
25. Seifi N, Kahani N, Askari E, Mahdipour S, Naderi NM. Inducible clindamycin resistance in Staphylococcus aureus isolates recovered from Mashhad, Iran. Iran J Microbiol 2012;4:82-6.
26. Cetin ES, Gunes H, Kaya S, Aridorogan BC, Demirci M. Distribution of genes encoding resistance to macrolides, lincosamides and streptogramins among clinical staphylococcal isolates in a Turkish university hospital. J Microbiol Immunol Infect 2010;43:524-529.
27. Westh H, Hougaard DM, Vuust J, Rosdahl VT. Prevalence of erm gene classes in erythromycin-resistant Staphylococcus aureus strains isolated between 1959 and 1988. Antimicrob Agents Chemother 1995;39:369-373.
28. Saderi H, Emadi B, Owlia P. Phenotypic and genotypic study of macrolide, lincosamide and streptogramin B (MLSb) resistance in clinical isolates of Staphylococcus aureus in Tehran, Iran. Med Sci Monit 2011;17:48-53.
29. Lina G, Quaglia A, Reverdy ME, Leclercq R, Vandenesch F, Ettienne J. Distribution of genes encoding resistance to macrolides, lincosamides, and streptogramins among staphylococci. Antimicrob Agents Chemother 1999;43:1062-1066.