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PREVALENCE OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* IN SAUDI ARABIA: SYSTEMIC REVIEW AND META-ANALYSIS

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ABSTRACT

In recent years, methicillin-resistant *Staphylococcucs aureus* (MRSA) have become a truly global challenge. Systemic review and meta-analysis was performed to summarize the prevalence of MRSA in different regions of Kingdom of Saudi Arabia (KSA). A search of the PubMed, Google and Google Scholar databases for studies published during the period of 1 January 2002 through 31 December 2012 was conducted. We included studies that looked at the number and prevalence of MRSA among total *S. aureus*. Meta-analyst and comprehensive meta-analysis were used for statistical analysis. Twenty six studies were included in the review, representing five regions of KSA. Pooled estimation of 22,793 *S. aureus* strains showed 35.6% (95% Confidence interval (CI), 0.28 – 0.42; P < 0.01) of the strains were MRSA with significant heterogeneity. Prevalence of MRSA ranged from 5.97% to 94% in Dahran and Riyadh cities, respectively. MRSA proportion among KSA regions is slightly high and varied from one city to the other.
Key words: Saudi – methicillin-resistant *Staphylococcucs aureus* -systemic review.

INTRODUCTION

S. aureus is a versatile human pathogen that causes diseases ranging from mild infection of the skin to life threatening sepsis (1). After introduction of penicillin in 1940, penicillinase-producing *S.aureus* were detected, leading to development of penicillinase-resistant semi-synthetic penicillins as methicillin and oxacillin. Within a year from this, MRSA were reported in United Kingdom (2). The emergence of strains resistant to methicillin and other antimicrobial agents has become major concern because of the higher mortality due to systemic MRSA infections (3).

Although the rates of isolation of MRSA have been increasing throughout the world for the last decades and in some areas the rates reached > 50%, there are considerable variations in the prevalence of MRSA according of geographic area (4,5,6).

KSA covers over 2 million Km^2 area and estimated population over 27 million and considered potentially hot spot for the collection of MRSA because up to 6 million of their populations are expatriates from many countries. In addition, KSA hosts about four million Muslim pilgrims from all over the world (7). KSA studies in the early 1990s consistently found low MRSA prevalence (5% and 7.5%) which increased dramatically up to 91% after 1995 (8). This study aims to determine average MRSA prevalence in KSA hospitals by conducting a systemic review and meta-analysis.

MATERIALS AND METHODS

Data acquisition: literature search was conducted in the PubMed and Google Scholar database for the time period spanning January 2002 to December 2012. The search strategy used keywords (and combinations thereof) "*Staphylococcus aureus*", "*S. aureus*", "Prevalence", "Methecillin"," Methecillin-resistant *Staphylococcus aureus*", "MRSA" and "Saudi Arabia". Additionally, abstract book of International congress on infectious Diseases was explored.

Inclusion and exclusion criteria:

The following features were included in the study:

1- *S. aureus* samples were collected from Saudi hospitals.

2- . Prevalence of infection or colonization with MRSA in patients or residents in clinical and nursing healthcare settings was reported.

Studies were excluded for the following reasons:

1- There were ≤ 2 cases of MRSA bacteremia reported.

2- The study described results that used previously published data with > 1 year of overlap or 75% time overlap between studies (in these cases, one representative study was chosen).

3- . Samples were partially/totally selected from MRSA culture collections. 4. Studies failed to focus on MRSA prevalence (these included studies those mixed results of " coagulase-negative Staphylococcus and *S. aureus* or healthy people and patients, estimating MRSA transmission, or The therapeutic efficacy

Data extraction

A data extraction form was developed to collect information from MRSA prevalence studies. This included study location, study period, specimens and/or sites, number of patients or specimens, and results present in form of proportions (express as the percentage of MRSA cases among isolates of *S.aureus*.

Statistical analysis

Statistical analysis was performed by the use of Meta-analyst (version 3.13 Beta) and Comprehensive Meta-Analysis (version 2.0) software. By using Meta-Analyst, overall proportion of MRSA in Saudi was pooled by forest plot with 95% confidence interval (95% CI). The Q statistic for homogeneity and the I^2 test were calculated to assess whether results varied no more than might have been expected by the play of chance

(random sampling). A significant heterogeneity was considered for P < 0.10 and I^2> 50% (9). The small study bias was measured by Begg's funnel plot and by the Egger test (10,11).

RESULTS

From January 2002 through December 2012, Twenty six published articles that matched inclusion criteria were selected for meta-analysis (12 - 37). Among these publications which reported the prevalence of MRSA in KSA, twenty five studies were represented five regions only (from thirteen total regions of KSA) and one study did not reported location (submitted as KSA) (Table 1). Study duration varied between 4 and 96 months whereas one and five days study period were reported in two publications (23,30). Most studies, screening was performed as multi-site swabbing, most often by additional swabs taken from skin lesions, nasal or wounds. While three studies did not mentioned screening sites only clinical specimen or pediatric and adult population reported (15,16,19).

As shown in Forest plot (Figure,1) sample size and 95% CI of each study was reported. Additionally, pooled estimation (Overall) of 22793 *S.aureus* showed 35.6% (95% CI, 0.28 – 0.42; P < 0.01) of strain to be MRSA. There was a high level of heterogeneity, random model methods (I^2= 100%, P <0.001). According to Begg and Mazumdar rank correlation test, a significant correlation suggests that bias exists but does not directly address the implications of this bias (Kindall s tau= -0.11) with a 1-tailed P-value = 0.20.

MRSA proportions variation ranged from 5.97% to 94.59% in Dahran and Riyadh cities, respectively (14,33). Average proportion of MRSA in different KSA regions reported that, Al-Gouf recorded <15% in contrast to highest prevalence in Assir and Riyadh (40%-60%) respectively. Makkah was positioned in intermediate value (25%-40%) as MRSA prevalence (Figure, 2).

TABLE 1: SUMMARY OF STUDIES REPORTING METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) IN HOSPITAL OF SAUDI ARABIA.

Location		Study period, (months)	Specimens and/or sites	No. of patients (P) or specimens (S)	No. of *S.aurius*	No. of MRSA (%)	Reference (1st author)
Region	Hospital (City)						
Al-Gouf	A/Sidery H. (Al-Gouf)	2008-2009 (9)	Urine	930 (S)	100	13(13)	Al-Ruaily (2011)
Al-sharqia	1-KF- H. 2-TCC. (Al-Hasa)	1999-2004	Wound-blood-sputum- eye-catheter	-	6765	161(2.37)	Panhotra (2005)
	SAMSO. (Daharan)	1999-2003 (60)	Skin- soft tissue- blood	-	5162	308(5.97)	Al-Tawfiq (2006)
	KA-H. (Al-Ahsa)	2006-2008	Pediatric and adult population	-	1930	463 (23.98)	Ahmed (2009)
	KF- H. (Alkhobar)	2002-2005 (44)	Clinical specimens	5534(S)	4063	1918(47.20)	Akhtar (2009)
	SAMSO. (Daharan)	2002-2006 (60)	Blood	1103 (P)	122	27(22.13)	Al-Tawfiq (2009)
	KF- UH. (Al-Khobar)	2001-2008 (96)	Soft tissues and invasion infection	-	633	243(38.38)	Bukharie (2010)
Assir	Assir CH. (Abha)	2003-2004 (6)	Clinical specimens	-	85	39(45.88)	Al-Azraqi (2005)
	1-Asir CH. 2-Abha GH., (Aseer)	2004 (7)	Wounds - abscesses -vaginal discharges.	9631(S)	200	86(43)*	Hamid (2011)
	Aseer CH. (Aseer)	2011 (6)	Nasal swab	81 (P)	81	50 (61.72)	Abdalla (2012)
Makkah	KA-UH. (Jeddah)	1998 (12)	Sputum- blood	111(p)	292	111(38.01)	Madani (2002)
	THNG. (Jeddah)	2002 5-day	Nasal swabs	240 (P)	240	10(4.16)	Austin (2003)
	Al-Hada AFH. (Taif)	2004 (12)	Blood - surgical urinary and respiratory tract infection- wounds	1382(P)	252	146(57.93)	Abdel-Fattah (2005)
	1-Al-Nour H. 2-KA-H. 3-Hera H. 4-KFl-H. (Makkah)	2004-2005 (12)	Blood	1626 (S)	303	161 (53.13)	Ashgar (2006)
	1-Al-Nour H. 2-KA-H. 3-Hera H. 4-KFl-H. (Makkah)	2003-2004 (12)	Wound- eye- respiratory tract - blood- urine – ear	124-132 (S) per hospital	512	199(38.86)	Ashgar (2006)
	1-Al-Nour H. 2-KA-H. 3-Hera H. (Makkah)	2008-2009 (12)	Blood- wound- respiratory tract and urinary tract infection- septicemia- eye- ear	1087(P)	688	271(39.38)	Asghar (2011)

	UH, Western region, (Makkah)	2009-2010 (12)	Wound – skin – soft tissues – pneumonia - eye- joint- sinus- catheter	186 (P)	200	79 (39.5)	El Amin (2012)
Riyadh	KK-UH. (Riyadh)	2004 (12)	Blood stream	220(P)	21	3(14.28)	Babay (2005)
	KF- National Guard H. (Riyadh)	2003 (1day)	Blood -surgical-urinary tract infection - pneumonias	121(P)	12	5(41.66)	Balkhy (2006)
	AFH. (Al-Kharj)	2004-2007 (36)	Pus- wound - ear - aspirates- sputum	689 (S)	166	37(22.28)	Ahmad (2009)
	KK-UH. (Riyadh)	2005-2008 (39)	Skin - soft tissues	280 (P)	280	80 (28.57)	Bukhari, (2009)
	KK-UH. (Riyadh)	2007	skin – soft tissues - abscess - cellulites-ulcers	-	37	35(94.59)	Moussa (2009)
	Specialist H. (Al-Kharj)**	2007 (4)	Nasal swabs	352 (S)	112	9(8.03)	Ahmad (2010)
	KK-UH. (Riyadh)	2005-2008 (48)	Skin and soft tissues - invasive infections	285 (p)	285	85 (29.82)	Al-Otaibi (2010)
	H. and HC. (Riyadh)	2008-2009	Wound – skin – soft tissues –lung abscess - pneumonia –fracture bone –burn - blood	-	135	127(94)	Moussa (2011)
KSA	-	2001-2004	Blood- nasal swabs tracheal aspiration- catheter- wound, sputum	-	117	24(20.51)	Tayfour (2005)

H= Hospital; UH= University hospital; GH= General hospital; HC= Health centers; CH= Central hospital; SH= Specialist Hospital; TCH= Tertiary-care hospital; TCC=Tertiary care center; AFH= Armed force hospital; AFH=Armed Forces Hospital; SAMSO = Saudi Aramco Medical Services Organization;THNG= teaching Hospital of national guard; KF= King Fahd; King Abdul-Aziz= KA; K.Fl.= King Faisal; KKESH= King Khaled Eye Specialist Hospital; * = environmental isolates were excluded; * *= Hospital not mention and write the author city; KSA = Kingdom of Saudi Arabia.

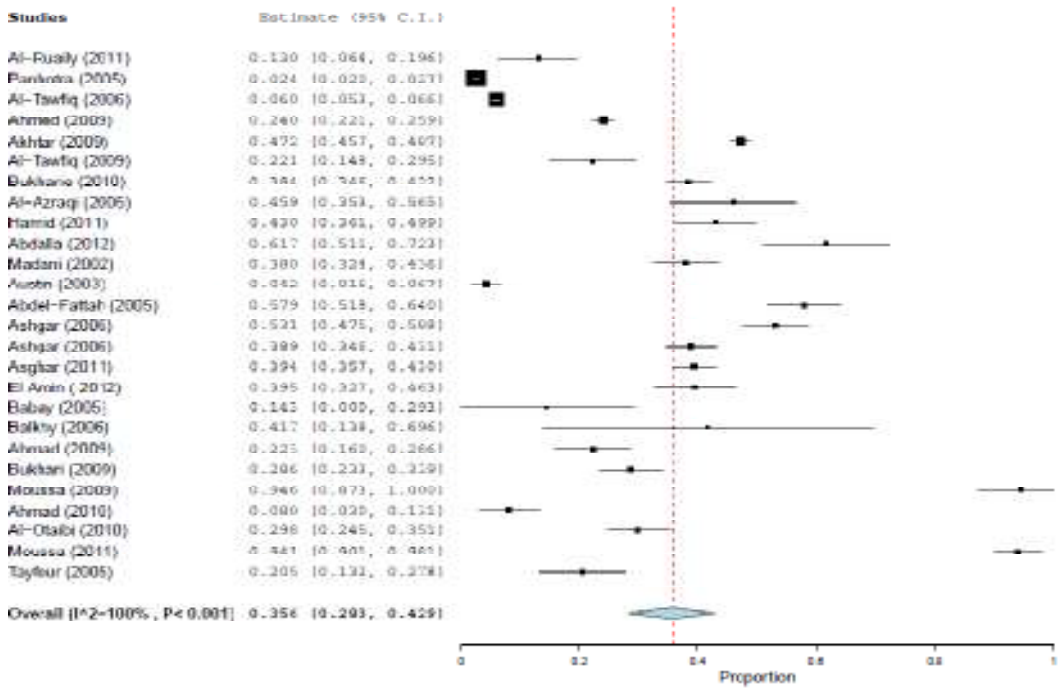

FIGURE 1: FOREST PLOT OF PROPORTION OF MRSA AMONG *STAPHYLOCOCCUS AUREUS* IN THE 26 SAUDI STUDIES, 2002-2012.

FIGURE 2: PROPORTIONS VARIATION OF MRSA IN SAUDI ARABIA, 2002-2012.

DISCUSSION

In this review, 26 studies on MRSA prevalence in different KSA regions were analyzed since 2002 to 2012. We summarized the cumulative prevalence of MRSA and supplied a map to explain the epidemiology of MRSA in Saudi.

According to our study, the overall estimation of MRSA prevalence in Saudi was 35.6% (95% CI, 0.28 – 0.42). whereas MRSA prevalence mean was different from region to another (Figure, 2). While, variation in MRSA proportion exists in several cities (5.97% to 94%). As we know, meta-analysis studies for MRSA prevalence in KSA are not reported but some studies mentioned MRSA average. MRSA proportion from KSA peer-reviewed studies between 1993 and 1997 is low (5-10%) (38). Recently, MRSA prevalence in Saudi is closely with our data where detected 29.9% from January 1990 through April 2011 (39). This finding indicates that temporal increases in MRSA prevalence in KSA. One major factor that could drive regional MRSA dissemination could be the ineffective of infection prevention. Although the reasons for variation of MRSA proportion in KSA cities are unknown, Van Belkum et al have looked at the clonal distribution of MRSA in various part of KSA and found that a single clone account 93% of examined isolates. Therefore it seems that difference in the incidence of MRSA reflects host or environmental factors (40). Additionally, high variation may be due to epidemiology of MRSA is in transition period and infection control rules may be most effective (41). In regional perspective, Saudi has a higher prevalence of MRSA than Bahrain, Kuwait, and Lebanon countries. In contrast, MRSA prevalence in Egypt, Oman, Iran and Jordan was reported more than 50% (39,42,43) . From an international stand, the mean incidence of MRSA across China was over 50% and in Shanghi, the prevalence was over 80% (44). In Spain, the prevalence of MRSA was 29.2% (45).

Limitations of the study

1- The studies we review contain data about different patient population (up to six million of whom are expatriates mainly from south and east Asia beside annually a host of Muslim pilgrims)
2- Only five KSA regions which cannot fully represent Saudi was pooled data
3- Due to limited access to in-press articles and theses, some studies might been missed beside low number of MRSA prevalence studies in KSA (26 studies).

Conclusion

Our study showed that MRSA proportion among KSA studies is slightly high and varied from one city to the other. Thus, to combat the MRSA dissemination, public health researchers and all health professionals must understand the role of hospital hygiene protocols and of antimicrobial drug policies, as well as mechanisms of regional spread of MRSA throughout hospitals. Future systematic reviews would also ideally be based on a greater number of studies that are of high quality.

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