Antimicrobial Susceptibility Pattern and Serotype Distribution of Streptococcus Pneumoniae in the Middle East Region: A Systematic Review and Meta-Analysis

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Received: 16 Jul. 2020; Accepted: 18 Dec. 2020

Abstract- This study aimed to explore the prevalence, antimicrobial resistance levels, and serotype distribution of *S. pneumoniae* in the Middle East region. We conducted a systematic literature review by searching several databases including PubMed, ISI Web of Science, Scopus, Google scholar through 2000 to 2017 by using the following keywords: "*Streptococcus pneumoniae*", "pneumococcus", "serotype", "Antibiotic resistance," and "Middle East "in combination with "OR" and "AND" Boolean Operators within Title/Abstract/Keywords fields. We used a random-effects model to calculate the pooled prevalence and 95% confidence intervals (CIs) for binomial variables. All statistical analyses were done using STATA 12.0 (STATA Corp, College Station, TX). We found 73 articles appropriate, on the word of inclusion and exclusion criteria, for inclusion in this systematic review and meta-analysis. The result revealed that the pooled prevalence of *S. pneumoniae* carriage was 35% (95% CI: 26-44%). The most frequent pneumococcal serotypes were19, 19F, 6, 23 and 6A/B which were found in 19%,12%, 11%, 10% and 10% of isolates respectively. Pneumococcal resistance reported for azithromycin, cefaclor, clarithromycin, chloramphenicol, erythromycin, and tetracycline were 24%, 37%, 23%, 11%, 26%, and 29% respectively, while vancomycin resistance was not reported. The highest resistant prevalence was reported against co-trimoxazole (Trimethoprim/sulfamethoxazole). For this antibiotic, a pooled resistance prevalence of 43% was identified. The present review demonstrates that the prevalence of *S. pneumoniae* carriage was high in the Middle East region. Surveillance must be continued in this region to evaluate. The resistance pattern and serotype distribution.

Acta Med Iran 2021;59(2):64-78.

Keywords: *Streptococcus pneumoniae*; Antimicrobial susceptibility; Serotype; Middle east

Introduction

Streptococcus pneumoniae is a common cause of community-acquired infections such as pneumonia, meningitis, otitis media, and sepsis (1,2). The organism is commensal in the upper respiratory tract but can cause infections in some conditions (2).

Based on the reports, despite the accessibility of efficient vaccines and antibiotics, pneumococcal diseases were annually responsible for nearly one to two million deaths worldwide (3). The increase of antibiotic-resistant microorganisms is a main concern to the public, and similar to other pathogens, resistance to several antimicrobial agents such as macrolides, penicillins, and

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cephalosporins have been expanded among pneumococci (1). This causes the treatment of pneumococcal disease to have a challenging consequence (1). Moreover, diverse pneumococcal serotypes display various antibiotic sensitivity (4). Based on the immunochemistry of the antigenic capsular polysaccharide, pneumococci are classified into more than 100 serotypes; of them, 15 serotypes are known to reason almost 90% of the invasive diseases around the world. This serotypes including 14, 6, 1, 19, 3, 4, 5, 9, 18, 23, 12, 7, 2, 25, and 8 serotypes (2,5). The polysaccharide capsule causes resistance to phagocytosis in the lack of type-specific antibody and has a major role in the pneumococcus invasion into the systemic blood system. Several serotype-specific pneumococcal polysaccharide and conjugate vaccines have been premeditated, which synthesize the capsular polysaccharides of the more common invasive serotypes (2,6). Because the distributions of the invasive serotypes vary geographically, knowledge of the regional pneumococcal serotype distribution is essential for a suitable vaccine program.

Therefore, comprehensive information about the epidemiology of pneumococcal resistance and serotype distribution is essential to monitor changing trends and attempt interventions to cease these trends. The prevalent serotype distribution and drug resistance patterns of *S. pneumoniae* had been investigated in the Middle East region with various studies, but similar data about the situation in this region have been sparse. Also, few studies have often been unrelated, using dissimilar methodologies and specimens; as a result, they are hard to compare. Therefore, this study focuses on the work undertaken in the Middle East region to evaluate the epidemiology of resistance and serotype distribution in *S. pneumoniae* isolates in this region.

Materials and Methods

Search strategy

A systematic review of the published literature was performed from 2000 to 2017. The following databases for relevant articles were searched without language limitations: Medline via PubMed, Scopus, Web of Science, and Google Scholar. The following keywords were used: "*Streptococcus pneumoniae*", "pneumococcus", "Serotype", "Antibiotic resistance" and "Middle East "within titles and abstracts in combination with "OR" and "AND" Boolean Operators in the Title/Abstract/Keywords fields. The data included in this review relate to the following 16 countries: Syria, Israel, Iran, Turkey, Saudi Arabia, Egypt, United Arab Emirates, Iraq, Qatar, Lebanon, State of Palestine, Jordan, Yemen, Oman, Bahrain, and Kuwait. One of our research team members evaluated the search results randomly and confirmed no related article was ignored. One of the team researchers (SK) screened the articles for the appropriateness of titles and abstracts. Any disagreements with article selection were resolved after discussion with the corresponding author (DA).

Inclusion and exclusion criteria

Studies with the following criteria were included in the study: 1) studies that investigate the prevalence of pneumococcal carriage from different areas of the Middle East region. 2) Studies published after 2000 were included. 3) Studies with sufficient information were provided in the context of serotypes distribution of antibiotic resistance patterns. Articles were excluded from the studies if Review articles, systematic reviews, case reports, and studies that did not have the minimum qualifications to be included in the meta-analysis. Finally, duplicate publications were excluded.

Quality assessment of studies

The quality of the relevant articles was assessed using a checklist for Prevalence Studies with the following items: sampling, sample size, setting, and valid methods, which was given by the Joanna Briggs Institute (7).

Data extraction

For all studies, the following details were extracted from the manuscripts: the first author's last name, publication date, the study setting, number of participants, study period, sample size, the source of isolates, research location, identification methods, antibiotic susceptibility testing method, serotyping methods, serotypes prevalence and proportion of antibiotic resistance. Three authors independently extracted data from included studies.

Statistical analysis

We calculated the prevalence estimates for each study and the corresponding pooled estimate using the Metaprop (8), a STATA-based command developed for binominal data. The 95% confidence intervals (CIs) were computed using the exact binomial method incorporating the Freeman-Tukey double arcsine transformation of proportions. Heterogeneity among studies was assessed by the DerSimonian & Laird Q test and I2 statistic which is the proportion of total variation due to between-studies heterogeneity.

Results

Literature search and study selection

A total of 610 articles were retrieved for consideration from database searches; the flowchart in Figure 1 shows the selection procedure for the involved studies. Of these, 384 papers were excluded due to duplication, and 226 articles were retained for the title and abstract assessment. Then, by reviewing the titles and abstracts, 128 articles were excluded. Finally, 73 articles had our inclusion criteria, which included a total of 14602 isolates (2,3,9-78). The list of articles included in this review is presented in Table 1.

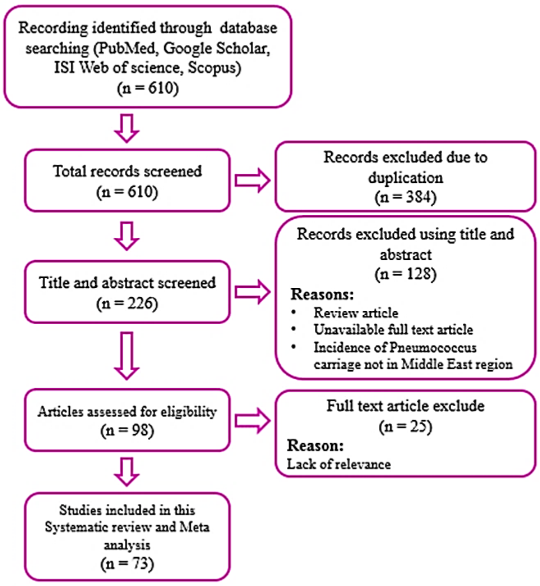


Figure 1. Flowchart for the selection procedure for inclusion of articles in the final analysis of the review

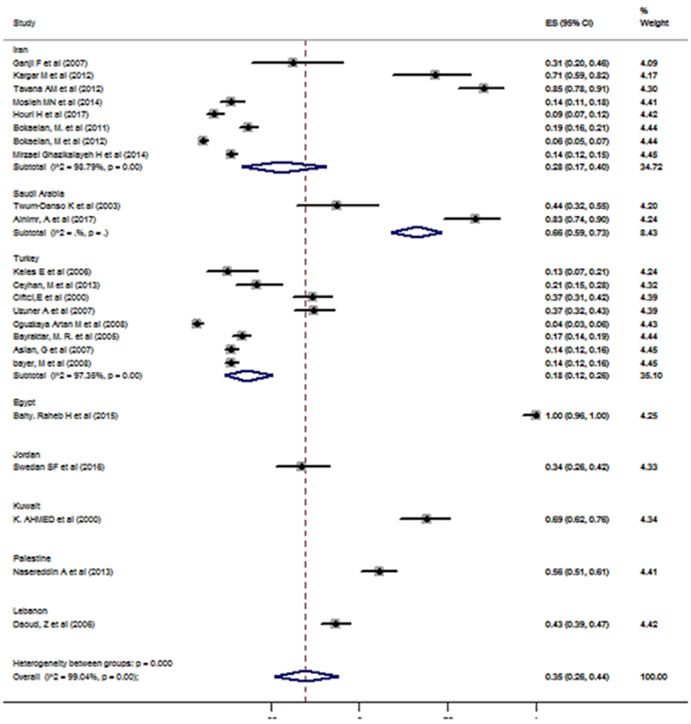


Figure 2. Prevalence of *S. pneumoniae* carriage in the Middle East region

Table1. The characteristic of the included studies

First author	Publication year	Country	Serotypes isolated
Al-Sheikh (2)	2014	Saudi Arabia	23F, 6B, 19F, 18C, 4, 14, 19A
Ahmadi (9)	2013	Iran	-
Ahmed (10)	2000	Kuwait	6B, 14, 19F, 23F
Alıskan (11)	2016	Turkey	-
Al-mazrou (12)	2005	Saudi Arabia	6, 19, 1, 15, 14, 23, 7, 18
Alnimr (13)	2017	Saudi Arabia	11A, 19A, 17F, 23F, 19F, 3, 14, 33, 6A, 8
Al- swailem (14)	2004	Saudi Arabia	19A, 6B,23F, 9V, 14,19F, 18C
Al- tawfigh (15)	2004	Saudi Arabia	-
Al- tawfigh (16)	2006	Saudi Arabia	-
Altınkanat (17)	2013	Turkey	19F, 23F, 6, 9V, 17F, 25F, 14, 18, 20, 22F, 23A, 3, 34, 4, 7B, 7C, 7F, 7A
Altun (18)	2006	Turkey	19, 14, 23, 9, 1, 6, 15
Altun (19)	2015	Turkey	3, 4, 6, 8, 9, 23,5, 6B, 7A, 9V, 20, 23F
Ashtiani (20)	2014	Iran	-
Aslan (21)	2007	Turkey	6, 19, 1, 23, 20, 17
Aslan (22)	2012	Turkey	-
Ataee (23)	2014	Iran	-
Bahy (24)	2016	Egypt	6A/B, 23F, 5, 19F
Bayer (25)	2008	Turkey	-
Bayraktar (26)	2005	Turkey	9, 19, 23, 10, 6 , 18
Bokaeian (27)	2011	Iran	1, 19A, 15C, 9V, 11A , 19F
Bokaeian (28)	2012	Iran	23F, 6B, 3, 19F , 14
Ceyhan (29)	2013	Turkey	6B, 9V, 14, 19F, 23F
Ciftci (30)	2000	Turkey	-
Dabboussi (31)	2013	Lebanon	-
Daoud (32)	2006	Lebanon	-
Daoud (33)	2011	Lebanon	-
Dashti (34)	2012	Iran	19, 6, 14, 17, 20, 23, 21
Elshafie (35)	2016	Qatar	3, 14, 1, 19a, 9v, 23F
Eltahawy (36)	2001	Saudi Arabia	-
Esel (37)	2001	Turkey	19, 23, 1, 3,6, 8, 14, 5, 18
Fouda (38)	2004	Saudi Arabia	9, 18, 23, 6, 19
Gunullu (39)	2000	Turkey	-
Gonullu (40)	2009	Turkey	-
Gildemir (41)	2016	Turkey	19F, 8, 1, 1 6A, 14, 23F, 5, 3,23A/B
Gur (42)	2001	Turkey	-
Gur (43)	2007	Turkey	-
Habibian (3)	2013	Iran	1, 2, 4, 6, 7, 19, 20, 8
Hanna-Wakim (44)	2012	Lebanon	19F, 6, 14, 9V/9A, 1, 3, 19A
Houri (45)	2017	Iran	23F, 19F, 19A, 9V, 11A, 14
Ilki et el (46)	2010	Turkey	-
Imani (47)	2007	Iran	-
Karam Sarkis (48)	2006	Lebanon	-
Kargar (49)	2012	Iran	-
Keles (50)	2006	Turkey	-
Kohanteb (51)	2007	Iran	-
Krishnappa (52)	2014	Saudi Arabia	23F, 19F, 14, 6B, 5, 6A, 19A, 9V
Memish (53)	2004	Saudi Arabia	19F, 9V, 4, 11, 6A, 3, 19A
Mirzaei (54)	2014	Iran	19F,6A, 15A, 11, 23F, 1, 19A, 35B
Mokaddas (55)	2007	Kuwait	-
Mokaddas (56)	2008	Kuwait	23F, 19F, 6A, 6B, 14, 19A.
Mokaddas (57)	2001	Kuwait	-
Mosleh (58)	2014	Iran	-
Nasereddin (59)	2013	Palestine	6A, 19F, 23F, 6B, 14, 19A,15B,34, 11A
Oguzkaya (60)	2008	Turkey	-
Oskoui (61)	2003	Iran	-
Özakin, (62)	2012	Turkey	-
Ozalp (63)	2004	Turkey	19, 23, 6, 9 ,15
Sener (64)	2007	Turkey	-
Senok (65)	2007	United Arab Emirates	-

Cont table 1.

Shibl (66)	2005	Saudi Arabia	-
Shibl (67)	2000	Saudi Arabia	-
Swedan (68)	2016	Jordan	19F, 6A/B, 11A, 19A, 14 ,15B/C
Taha (69)	2012	Lebanon	19F , 23 , 2 , 14, 19A , 12F
Tavana (70)	2012	Iran	6,19
Telli (71)	2011	Turkey	19.23,6,14,15
Twum-Danso (72)	2003	Saudi Arabia	6,19,1,15,14,23
Uncu (73)	2007	Turkey	-
Uwaydah (74)	2006	Lebanon	-
Uzuner (75)	2007	Turkey	-
Yalcin (76)	2006	Turkey	19F, 6B,23F,23,1
Yenisehirli (77)	2003	Turkey	19,23,9,14,6
Yurdakul (78)	2001	Turkey	-

Identification and validation of *S. pneumoniae* isolates

Overall, among 73 studies included in this meta-analysis, 33 studies reported the serotypes of *S. pneumoniae*; among them, 26 studies performed quellung reaction as the serotyping method, and ten studies used the molecular typing method (Multiplex PCR) for pneumococcus serotyping. Moreover, three studies used both Multiplex PCR and quellung reaction for the serotyping purpose (2,13,44).

Serotype distribution of *S. pneumoniae* isolates

Thirty-three studies reported the serotypes of *S. pneumoniae*. A total of 5349 isolates recovered from various samples. The predominant serotypes were 19, 19F, 6, 23 and 6A/B, which were belonged to 19%, 12%, 11%, 10% and10% of isolates, respectively (Table 2). Of the 5349 isolates in the14 studies (9%) were identified as non-typeable serotypes.

Our analysis revealed substantial variations in the proportions of serotypes across geographical regions. The most prevalent serotypes identified in Iran were 6A, 19F, 6, 19, 6B, 2, and 15C which were found in 19%,16%,11%,10%,9% and 9% of isolates, respectively. Among 12 studies from Turkey, the predominant serotypes were 19F, 19, 23, and 23F, which were found in 12%, 21%, 10%, and 7% of isolates, respectively. The majority of Turkish studies were carried out from 2001 to 2015. All in all, seven studies were retrieved from Saudi Arabia from 2004 to 2014 in which the most prevalent serotypes were 23F, 19F, 19, 23, 6, and 6B, which were found in 10%, 7%, 21%, 10%, 19% and 7% of isolates, respectively. Serotype 23F and 19F were represented in all studies.

Antibiotic resistance profiles of *S. pneumoniae* isolates

Overall, 70 studies were recognized that reported antibiotic resistance pattern in *S. pneumoniae* isolates. The highest resistance rate was reported against co-trimoxazole. For this antibiotic, a pooled resistance proportion of 43% (95% CI; 34 %-53%) was identified. The prevalence of pneumococcal resistance to imipenem was 1% (95% CI; 0% -2%), which was the lowest proportion of antibiotic resistance. The prevalence of pneumococcal resistance to penicillin was 14% (95%CI; 10 %-18 %) (In 61 studies). Reported resistance for azithromycin, cefaclor, clarithromycin, chloramphenicol, erythromycin, and tetracycline was 24% (95%CI; 15 %-34%) (12 studies), 37% (95% CI; 22%-53 %) (7 studies), 23% (95% CI; 14%-33 %) (13 studies), 11% (95% CI; 8%-15%) (28 studies), 26% (95% CI; 21%-32%) (54 studies) and 29% (95% CI; 23%-36%) (35 studies), respectively (Figures 3-5).

Seven studies were identified from Turkey between 2000 to 2016 in which the highest resistance prevalence estimates were found to co-trimoxazole, tetracycline, cefaclor, erythromycin, clindamycin, azithromycin, and ciprofloxacin, which identified in 32% (15 studies), 24% (14 studies), 19% (2 studies), 18% (22 studies), 18% (9 studies), 17% (6 studies) and 13% (5 studies), respectively.

In Iran, among isolates collected from 2003 to 2017, the penicillin resistance was 23%. In 14 studies retrieved from Iran, about 33%, 32%, and 32% isolates were resistant to co-trimoxazole, erythromycin, and tetracycline.

In Saudi Arabia, by 12 studies published in 2000 to 2017, the pooled resistance prevalence was 19% to a penicillin (12 studies), 68% to co-trimoxazole (7 studies), 33% to erythromycin (8 studies), 23% to tetracycline (3 studies), 16% to clarithromycin (3 studies) and 16% to cefotaxime (3 studies).

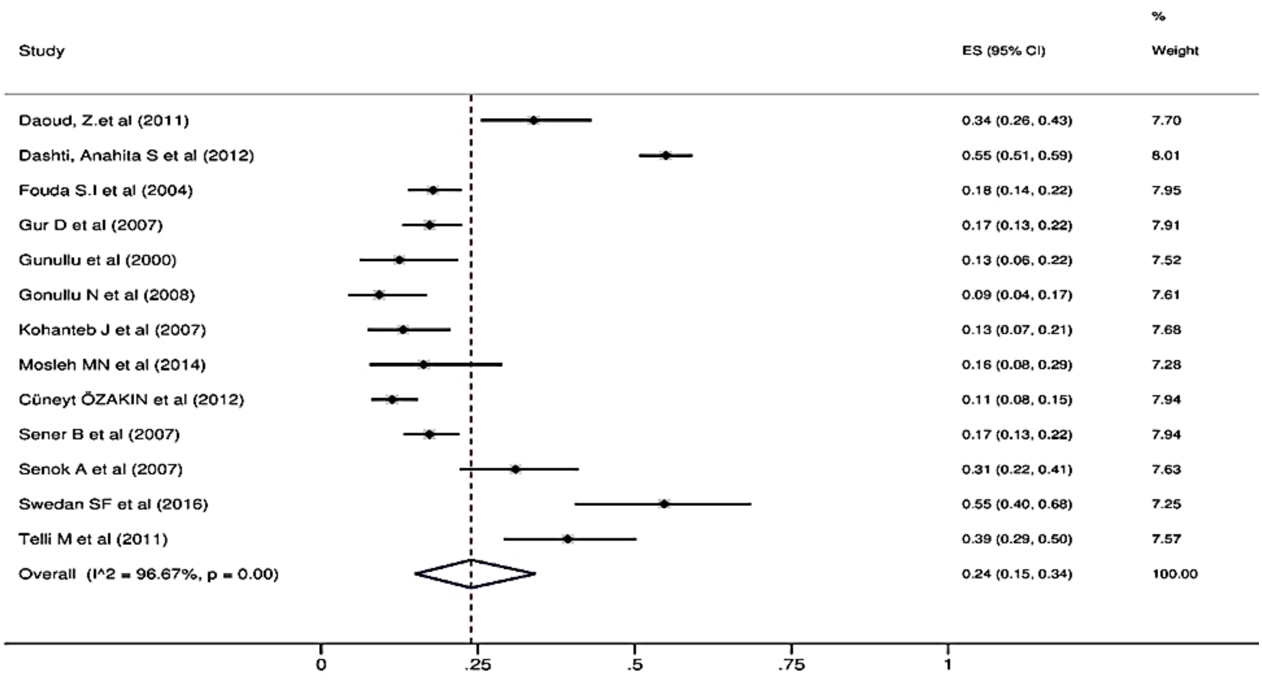
Among five studies from Kuwait, published in 2000 to 2010, around of 22% (5 studies), 48% (2 studies), 42% (2 studies), 32% (2 studies), and 21% (2 studies) were resistant to penicillin, co-trimoxazole, erythromycin, tetracycline, and cefuroxime, respectively.

Table 2. The pooled prevalence of different Serotypes of *S. pneumoniae* isolates

Serotype/serogroups*	No of studies	Pooled Prevalence	*P* of Q test
14	32	0.06	<0.001
3	23	0.05	<0.001
1	23	0.05	<0.001
19F	22	0.12	<0.001
23F	21	0.08	<0.001
19A	19	0.05	0.07
4	18	0.03	<0.001
6	15	0.11	<0.001
5	15	0.03	<0.001
8	15	0.02	0.01
6B	13	0.07	<0.001
9V	13	0.04	0.11
19	13	0.19	<0.001
23	13	0.10	<0.001
20	12	0.03	<0.001
15	11	0.05	<0.001
6A	11	0.07	<0.001
18	11	0.03	<0.001
18C	10	0.03	<0.001
7	9	0.02	<0.001
7F	9	0.02	0.03
22	8	0.03	0.03
9	8	0.07	<0.001
11	8	0.03	<0.001
11A	7	0.05	<0.001
10	7	0.02	0.06
2	7	0.04	0.01
17	7	0.03	<0.001
17F	6	0.03	0.01
33F	6	0.01	0.06
34	6	0.02	<0.001
23A	5	0.02	0.04
35B	5	0.02	0.29
15A	5	0.04	<0.001
9A	4	0.04	0.56
13	4	0.01	0.07
9V/A	4	0.03	0.23
6A/B	4	0.10	<0.001
10A	4	0.01	0.67
22F	4	0.02	0.01
18F	3	0.01	NA
29	3	0.01	NA
15B	3	0.01	NA
33	3	0.03	NA
12F	3	0.02	NA
15B/C	3	0.03	NA
16F	3	0.01	NA
23B	3	0.01	NA
19C	2	0.02	NA
24	2	0.01	NA
22F/A	2	0.02	NA
16	2	0.03	NA
7F/A	2	0.02	NA
7A	2	0.03	NA
15C	2	0.03	NA
21	2	0.05	NA
9L/N	2	0.01	NA
23A/B	2	0.02	NA
11A/D	2	0.02	NA
31	2	0.00	NA
9L	2	0.01	NA

Cont table 2.			
19B	2	0.00	NA
G	2	0.08	NA
32A	1	0.01	NA
25	1	0.03	NA
25F	1	0.05	NA
7B/C	1	0.02	NA
12	1	0.02	NA
10F/A/B/C	1	0.01	NA
33F/A/B/C	1	0.01	NA
38	1	0.01	NA
17A	1	0.01	NA
7B	1	0.00	NA
11C	1	0.00	NA
28A	1	0.01	NA
35	1	0.00	NA
37	1	0.00	NA
47	1	0.00	NA
33F/A/37	1	0.01	NA
15A/F	1	0.02	NA
38/25A/F	1	0.02	NA
7C/B/40	1	0.02	NA
24A/B/F	1	0.01	NA
35F/47F	1	0.01	NA
8F	1	0.02	NA
35F	1	0.02	NA
11A/14	1	0.02	NA
18A	1	0.01	NA
12A	1	0.01	NA
12B	1	0.01	NA
Non-typeable	14	0.09	<0.001

*; Items with number and letter are defined as serotypes, itemes with numbers refer to serogroupes. Note: in some studies the type of serotypes have not been determined and the serogroupes of isolates have just been characterized



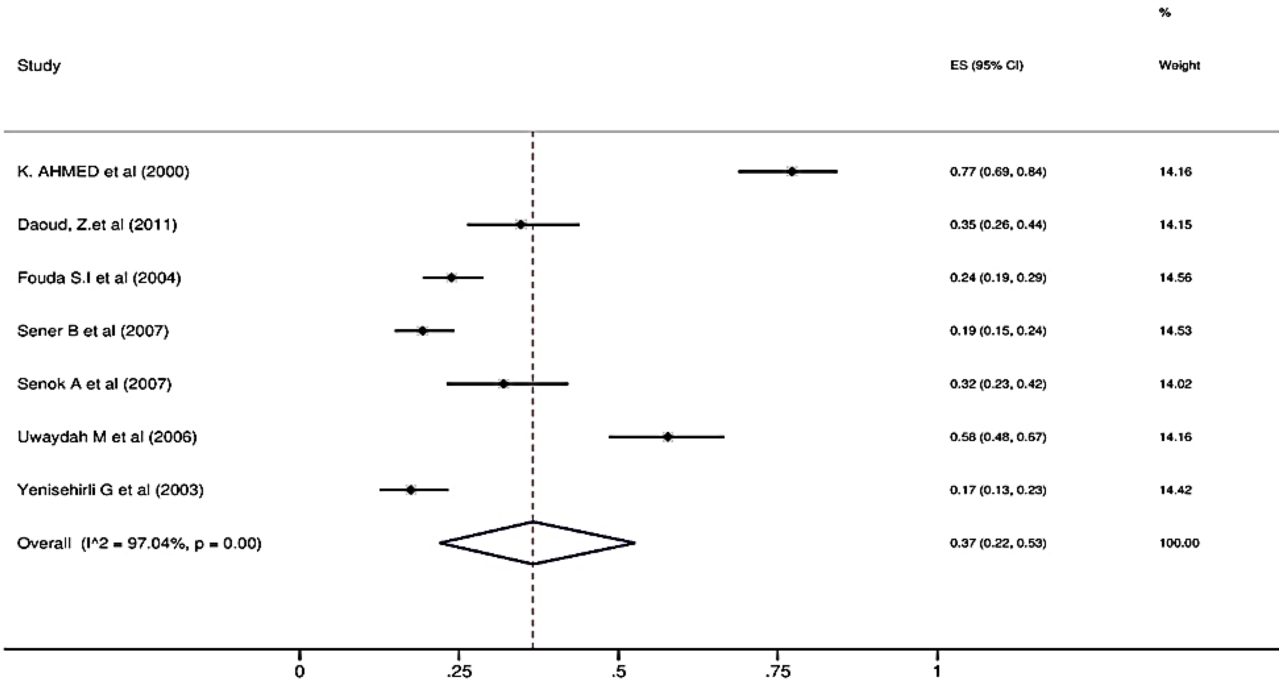
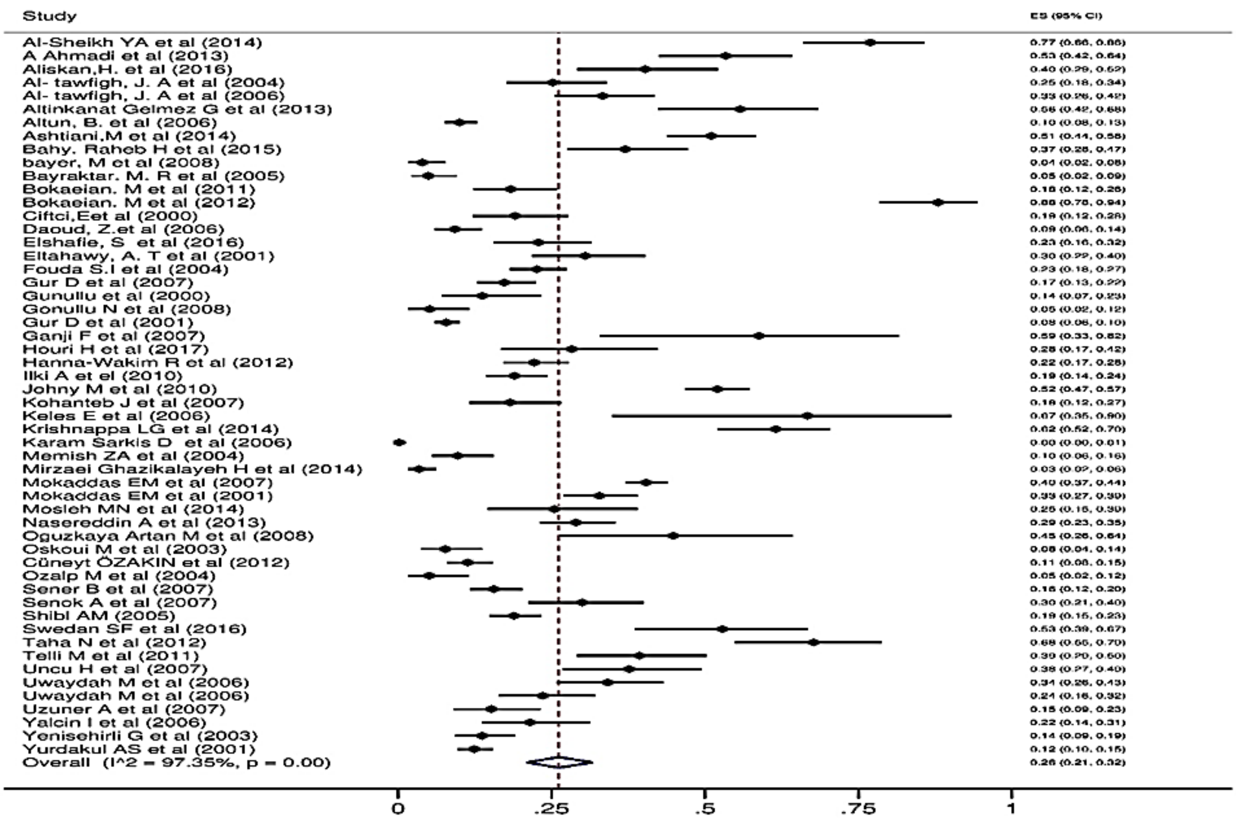


Figure 3. Forest plot of the meta analysis of antibiotic resistant among *S. pneumoniae* isolates. Azithromycin (upper) and Cefaclor(lower)



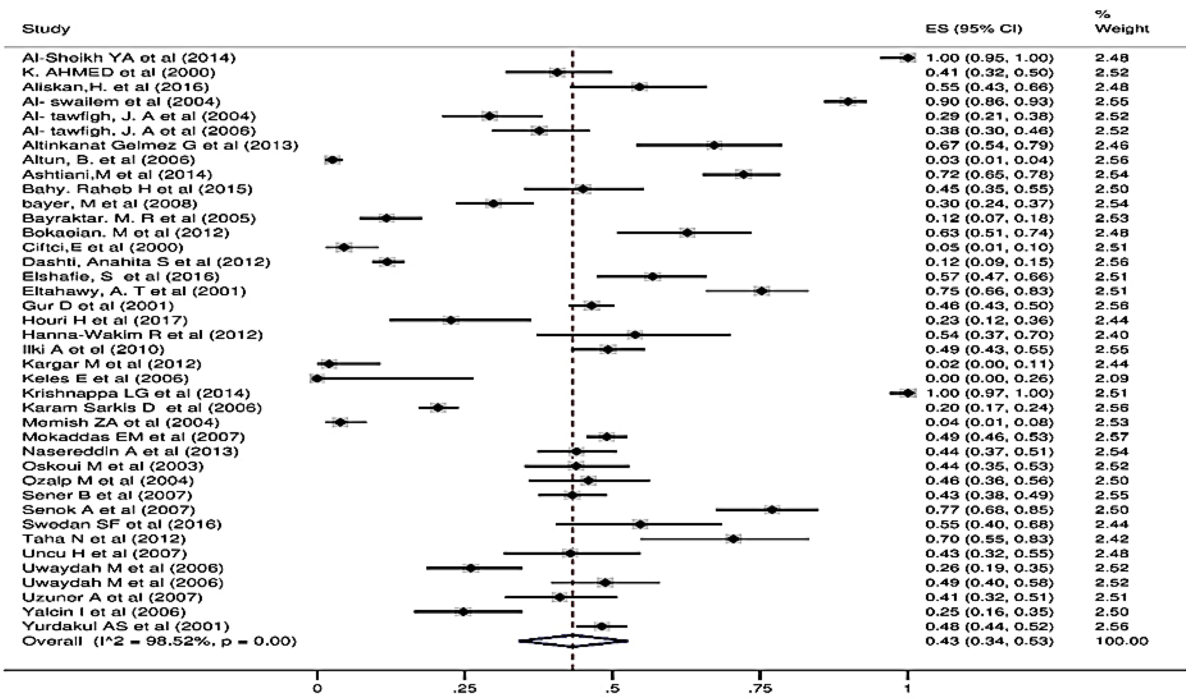
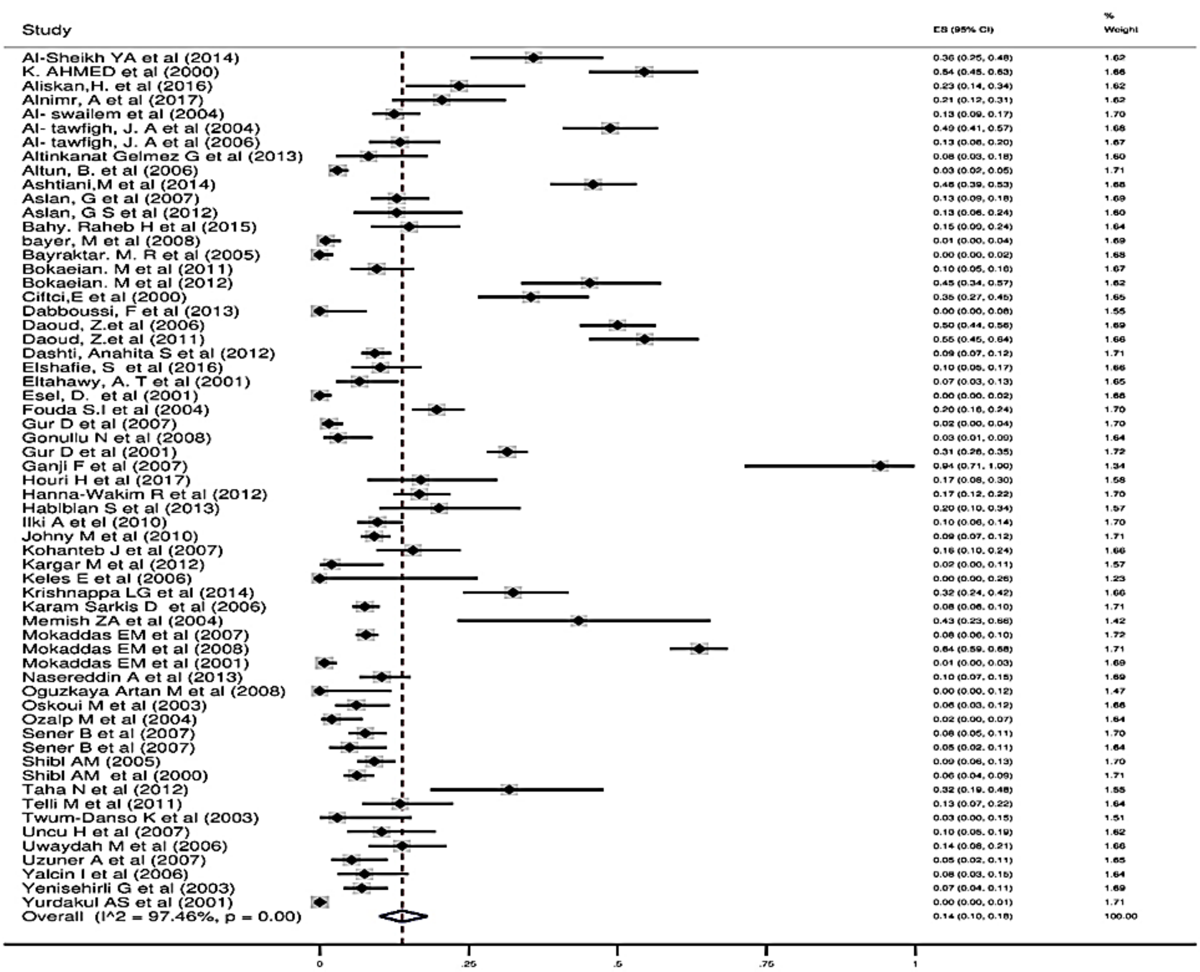


Figure 4. Forest plot of the meta analysis of antibiotic resistant among *S. pneumoniae* isolates. Erythromycin (upper) and Co-trimoxazole(lower)



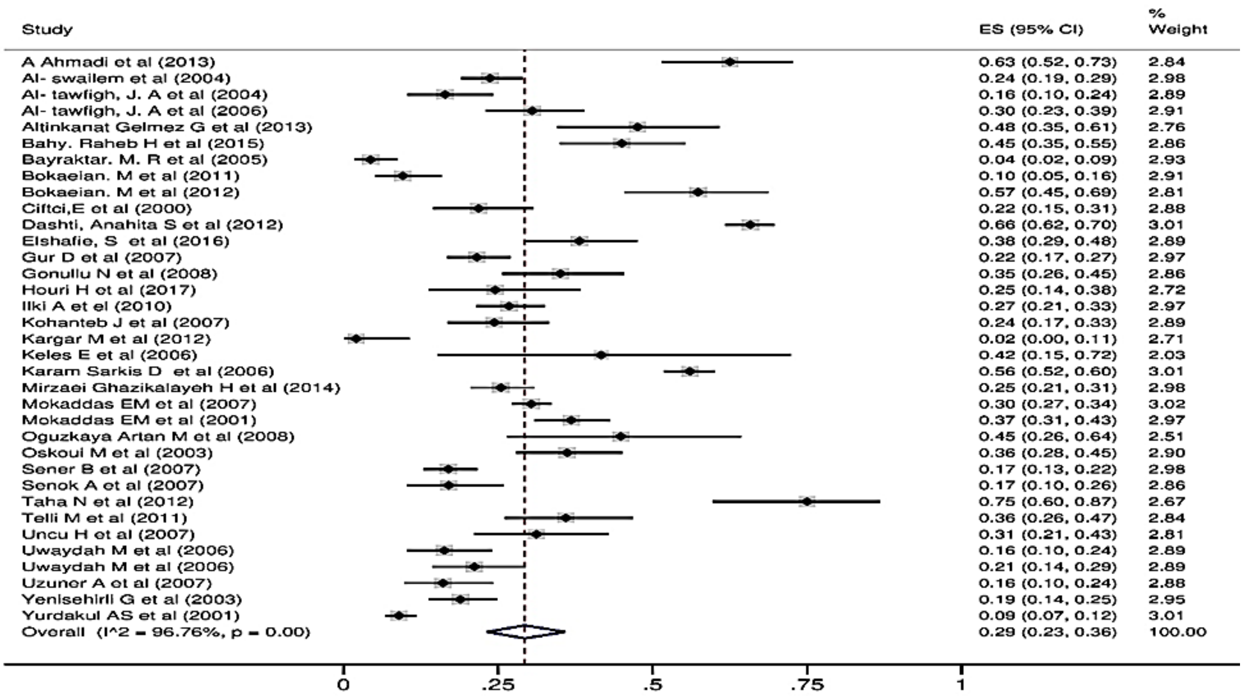


Figure 5. Forest plot of the meta analysis of antibiotic resistant among *S. pneumoniae* isolates. Penicillin (upper) and Tetracycline (lower)

Table 3. The pooled antibiotic resistance among all *S. pneumoniae* isolates

Antibiotic	No of studies	Pooled Resistance proportion	P of Q test	I^2
Ampicillin	8	0.08	<0.001	97%
Azithromycin	13	0.24	<0.001	97%
Cefazolin	2	0.09	NA	NA
Cefepime	1	0.08	NA	NA
Cefixime	1	0.20	NA	NA
Ceftriaxone	26	0.04	<0.001	90%
Cefuroxime	12	0.18	<0.001	96%
Clindamycin	16	0.16	<0.001	94%
Imipenem	6	0.01	<0.001	77%
Linezolid	7	0.00	<0.001	84%
Meropenem	2	0.00	NA	NA
Moxifloxacin	2	0.00	NA	NA
Ofloxacin	10	0.04	<0.001	86%
Penicillin	61	0.14	<0.001	98%
Tigecycline	2	0.03	NA	NA
Trimethoprim	1	0.38	NA	NA
Vancomycin	34	0.00	<0.001	60%
Amoxicillin-clavulanate	12	0.02	<0.001	88%
Amikacin	1	0.52	NA	NA
Aztreonam	1	0.26	NA	NA
Cefaclor	7	0.37	<0.001	97%
Cefamandole	1	0.00	NA	NA
Cefdinir	1	0.15	NA	NA
Cefotaxime	23	0.04	<0.001	93%
Cefprozil	3	0.05	NA	NA
Ceftazidime	2	0.17	NA	NA
Chloramphenicol	28	0.11	<0.001	95%
Ciprofloxacin	11	0.02	<0.001	83%
Clarithromycin	13	0.23	<0.001	97%
Cloxacillin	1	0.02	NA	NA
Co-trimoxazole	40	0.43	<0.001	99%
Erythromycin	54	0.26	<0.001	98%
Levofloxacin	15	0.00	<0.001	86%

Cont table 3.				
Nalidixic acid	1	0.02	NA	NA
Norfloxacin	1	0.44	NA	NA
Oxacillin	5	0.43	<0.001	99%
Piperacillin	1	0.00	NA	NA
Rifampin	5	0.01	<0.001	98.4%
Roxithromycin	1	0.18	NA	NA
Spiramycin	1	0.18	NA	NA
Telithromycin	4	0.00	0.27	23%
Tetracycline	35	0.29	<0.001	97%

Discussion

This systematic review provides a summary of the prevalence, distribution of serotypes, and the antimicrobial Susceptibility Pattern of *Streptococcus pneumoniae* in the Middle East region. The prevalence of the pneumococcal nasopharyngeal carriage rate significantly varies by geographically in the Middle East region. The highest and lowest rates of the pneumococcal nasopharyngeal carriage were reported from Egypt and Turkey, which was 100% and 4%, respectively (60). Moreover, there are limited studies about nasopharyngeal carriage in other countries such as Egypt, Jordan, Kuwait, Palestine, Syria, United Arab Emirates, Iraq, Yemen, Oman, Bahrain, and Lebanon. Therefore, these data may not be enough to reflect the pneumococcal carriage prevalence in these countries, and more studies are needed in these areas.

The most frequent serotypes in young children's carriage before the introduction of pneumococcal conjugate vaccines (PCVs) in low (64.8%) and lower-middle-income countries (47.8%) were 6A, 6B, 19A, 19F, and 23F (79). After the introduction of PCVs, the rates of vaccine-type carriage and Invasive Pneumococcal Disease (IPD) decreased (80), but the rates of colonization by non-vaccine-type of *S. pneumoniae* increased (80).

Serogroup 19 and serotype 19F were the most prevalent and represented in most of the geographical regions in the Middle East. Serogroup 19 is one of the common causes of outbreaks and has been reported in several invasive diseases such as otitis media (81). Before the introduction of PCV7, most of the IPD was caused by serogroups 19, 6, 14, and 18 in children less than five years, and also, the main cause of IPD among adults was serotype 3. After the introduction of PCV7, serotypes 19A and 3 were prevalent in young children and adults, respectively. Serotypes 19A and 19F were associated with invasive disease and mortality rates worldwide. Serotype 19A is also associated with resistance to penicillin, and according to the Asian Network for Surveillance of Resistant Pathogens (ANSORP) report, it is prevalent in Asian countries, and 28% of penicillin-resistant strains belong to this serotype (82).

Serotype 23F is another most common serotype in the Middle East and was included in the PCV7. This serotype had a high incidence in this area and other regions, such as Africa and Asian countries, where no conjugate vaccine has been introduced (83).

In the present systematic review, pneumococcal macrolide resistance was reported for azithromycin (24%), clarithromycin (23%), and erythromycin (26%). The erythromycin resistance rate in Kuwait, Saudi Arabia, Iran, Lebanon, and Turkey was 42%, 33%, 32%, 22%, and 18%, respectively. The macrolide resistance rate is varied in different countries, and between 20% and 40% of the pneumococcal isolates is macrolide-resistant [84]. Higher rates of macrolide resistance have been reported in East Asia countries such as China (95%) and Japan (>95%) (85,86). The pooled resistance prevalence of co-trimoxazole was 43%. Generally, pneumococcal antibiotic resistance in the Middle East countries has increased in recent years, and according to the World Health Organization (WHO) report in 2015, in most of these countries, antibiotic resistance Surveillance programs have not performed (87).

Antibiotic resistance among pneumococcus isolates is accelerated in the Middle East area in recent years. In the present study, the highest rate of resistance among pneumococcal isolates was against co-trimoxazole, while the lowest proportion of antibiotic resistance was against imipenem. It seems that the use of co-trimoxazole as a treatment regimen in the pneumococcal infections will not be useful. The common serotypes in the Middle East region were 19, 19F, 6, 23, and 6A/B serotypes, which are included in pneumococcal conjugate-vaccine. This data shows that pneumococcal conjugate vaccines (PCVs) can be effective against invasive pneumococcal infections in the Middle East region.

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