Prevalence and Incidence of carbapenem-resistant K. pneumoniae colonization: systematic review and meta-analysis

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Abstract

**Background:** *Klebsiella pneumoniae* is a gram-negative rod belonging to the order Enterobacterales and having a wide distribution in the environment, including the human colon. Recently the bacterium is one of the known problems in the healthcare setting as it has become resistant to last-resort drugs like carbapenems. The colonized person can serve as a reservoir for his/herself and others, especially in the healthcare setting leading to nosocomial and opportunistic infections. Therefore, we aimed to quantitatively estimate the rate of prevalence and incidence of colonization with carbapenem-resistant *K. pneumoniae*.

**Methods:** A literature search was conducted on PubMed/MEDLINE, Google Scholar, Science Direct, Cochrane Library, WHO Index Medicus, and others. All studies (published and unpublished) addressing the prevalence/ incidence of *K. pneumoniae* colonization were included in the study. Data were extracted onto format in Microsoft Excel and pooled estimates with 95% confidence interval calculated using Der-Simonian-Laird random-effects model. The degree of heterogeneity was presented with I2 statistics and prediction intervals. Publication bias was presented with funnel plots of standard error supplemented by Egger's tests.

**Results:** A total of 35 studies were included in the review and 32 records with 37,661 patients for assessment of prevalence while ten studies with 3643 patients were used for incidence of colonization. The prevalence of colonization with carbapenem-resistant *K. pneumoniae* ranges from 0.13% to 22% with variation in different localities with a pooled prevalence of 5.43% (3.73-7.42). Whereas the incidence of colonization ranges from 2% to 73% with a pooled incidence of 22.3% (CI: 12.74-31.87), both prevalence and incidence reports are majorly from developed countries. There was a variation in the distribution of carbapenem resistance genes among colonizing isolates with KPC as a major gene reported from many studies and NDM being reported mainly by studies from Asian countries. A univariate meta-regression analysis indicated continent, patient type, study design, and admission ward do not affect the heterogeneity (p-value>0.05).

**Conclusion:** The review revealed that colonization with *K. pneumoniae* is higher in a healthcare setting with variable distribution in different localities, and resistance genes for carbapenem drugs also have variable distribution in different geographic areas.

Background

*K. pneumoniae* is an omnipresent Gram-negative, non-motile bacterium belonging to the Enterobacterales order. It is a common bacterium in the colon and an opportunistic pathogen capable of causing many infections in mammals. Initial colonization is commonly from environmental sources (soil, water, animals, and vegetation) [1]. Despite its dissemination in the environment, the human gut is often a reservoir of *K. pneumoniae* [2]. *K. pneumoniae* colonizes following primocolonizer, but the timing of gut colonization is not known [3].

Classic *K. pneumoniae* is one of the frequent causes of nosocomial urinary tract infections [4], which are the most common among the older population and immunodeficient patients [5]. Hypervirulent *K. pneumoniae* strains, on the other hand, can cause invasive infections with severe complications in immunocompromised and healthy individuals [6].

Carbapenems possess broad-spectrum antibacterial activity and have a unique structure that is defined by a carbapenem coupled to a β-lactam ring which confers protection against most β lactamases such as Metallo-β-lactamase (MBL) as well as extended-spectrum β-lactamases [7]. Carbapenem-resistance is one of the foremost public health concerns as these drugs are the last resort drugs for treating drug-resistant bacteria [8, 9], like in the case of carbapenem-resistant (CR) Enterobacterales [10]. Currently, the global health care system is burdened by the high prevalence of carbapenem-resistant Enterobacterales (CRE), especially Klebsiella pneumoniae and Escherichia coli isolates [11-14].

The production of carbapenemases is one of the main mechanisms for the resistance of CRE strains. Carbapenemases are β-lactamases using carbapenems as hydrolysis substrates, including Ambler classes A, B, and C enzymes. Besides, these strains can also produce ESBLs and/or AmpC enzymes as well as lose outer membrane porin (OMP) proteins [15].

This study is aimed to quantitatively estimate the colonization rate of carbapenem-resistant *K. pneumoniae* from fecal samples.

**Methods**
Identification of records, screening of titles and abstracts, and evaluation of full texts for inclusion was performed following the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) flow diagram [16]. PRISMA checklist [17] was strictly followed throughout this systematic review.

**Identification of records and search strategy**

We have set a predetermined search strategy using PICO (Population, Interventions, Comparison, and Outcome). Accordingly, we have looked for all populations with the colonization of carbapenem-resistant *K. pneumoniae*, and intervention and comparison are not applicable as we intend to look for prevalence and incidence.

Literature was searched on electronic databases and indexing services like PubMed/MEDLINE, Science Direct, and other supplementary sources like WHO Index Medicus, Google Scholar, and Cochrane library. Advanced search, on major databases, was applied to retrieve relevant findings closely related to colonization with carbapenem-resistant *K. pneumoniae*. Carefully selected keywords and indexing terms were used to aid the search. The selected keywords included "*K. pneumoniae* [MeSH], Carbapenem [MeSH], carrier state [MeSH], Asymptomatic infections [MeSH] "carbapenem-resistant", carriage, colonization, carbapenemase, "carbapenemase producer", "carbapenem non-susceptible", and CRE. Boolean operators (AND, OR), truncation, and MeSH, and key terms were used appropriately for the systematic identification of records for the research question. The search was conducted from August 14 – 19, 2021, and all published and unpublished articles available online till the day of data collection were considered. Gray literature from organizations and online university repositories were accessed through Google Scholar with the help of Harzing's publish or perish 7.0 program.

**Screening and eligibility of studies**

Identified records were exported to ENDNOTE reference software version 20.0.1 (Thomson Reuters, Stamford, CT, USA) with compatible formats. Records with duplication were traced, documented, and removed with ENDNOTE and manually due to variation in referencing styles across sources. Afterward, the title and abstract of the article were screened with predefined inclusion criteria and full texts evaluation for eligibility.

**Inclusion and exclusion criteria**

There were predefined inclusion-exclusion criteria to come up with the final included articles during the initial screening of titles and abstracts and evaluating full texts for eligibility. Community members or patients with intestinal colonization of carbapenem-resistant *K. pneumoniae* were the study participants. Both retrospective and prospective studies addressing the prevalence or incidence of colonization with carbapenem-resistant *K. pneumoniae* were included regardless of the participants/ patient clinical characteristics. Online records published in the English language were considered for further eligibility assessment.

Review and original articles dealing with infection were excluded during the initial screening. Records were excluded when missing or incomplete outcomes, unrelated outcome measures, and inaccessible full texts (after requesting authors via email and/or Research Gate) were excluded. We have utilized the following case definitions for prevalence and incidence of colonization

- For the incidence of CRKP colonization: a patient who is negative for CRKP stool culture at admission and have a culture-positive result at any time after admission within a setting
- For the prevalence of CRKP colonization: A patient who is positive for stool culture before admission to setup, at admission, or community

**Data extraction**
Important data related to study characteristics (country, first author, year of publication, study design, participants characteristics, study setup, number of culture-positive results (bacterial), nature of drug resistance genes), and outcome of interest (number of carbapenem-resistant culture-positive results) were extracted using data abstraction format prepared in Microsoft Excel (Sheet 1).

**Critical appraisal of studies**

Critical appraisal to assess the internal (systematic error) and external (generalizability) validity of studies and to reduce the risk of biases was conducted according to the Joanna Briggs Institute critical appraisal tools for prevalence study, case-control study, and cohort studies [18, 19] and graded.

**Data processing and statistical analysis**

Relevant data extracted onto format in Microsoft Excel and exported to STATA 16 for analyses of outcome measures. DerSimonian and Laird's random-effects model was applied for the analyses at a 95% confidence level considering variation in true effect sizes across the population (clinical heterogeneity). Heterogeneity of studies was determined using $I^2$ statistics and predictive interval. A univariate meta-regression model was performed on study characteristics to assess the possible source of heterogeneity. Egger's test was used to evaluate the presence of publication bias and presented with funnel plots of the standard error of proportions [20]. A p-value less than 0.05 (one-tailed) was considered a cutoff point for statistical significance.

**Outcome measurements**

The primary outcome measure is the prevalence and incidence of colonization with carbapenem-resistant *K. pneumoniae*.

**Results**

**Characteristics of included studies**

We performed a systematic review following the PRISMA statement [16], and after the initial search of electronic databases and resources, a total of 2202 records were identified from several sources. From these, 175 were duplicate articles occurring in multiple databases and removed with the help of ENDNOTE and manual tracing. The remaining 2027 records were screened based on their titles and abstracts, and 1689 of them were excluded as the title and abstract are not related to the outcome variable and 45 were excluded due to language. Full texts of 293 records were then evaluated for eligibility, and 245 articles were also excluded as the outcome of interest was missing, insufficient, and/or ambiguous. Thirty-five articles were included in the study after passing the quality assessment and eligibility criteria (Figure 1) of these thirty-two studies, were used for the analysis of prevalence, and only ten studies for incidence since the studies have reported regarding colonization after admission to a setting.

**Study characteristics**

As shown in Table 1, a total of 35 studies with 37,661 participants were included for systematic review. Ten of the included studies were cohort studies [21–29] and 4 of them case-control [30–33], while the rest were cross-sectional studies. Two studies [34, 35] have included outpatients while the rest were conducted on admission and after admission to a setting. Joanna Briggs Institute scoring scale was used to rank studies, and the average quality scores of studies ranged from 5 to 8 (Supplementary file). All studies have applied standard microbiological and molecular techniques. Concerning the country of study, 19 studies were from Asia (8 studies from China and India), ten studies from Europe, two studies from Africa, and four studies from America (Figure 2). It is found that almost none of the studies were published before 2010, and the majority of them were published from 2017-2021 (more than 50%). For all studies, the rectal swab was utilized to study the colonization with carbapenem-resistant *K. pneumoniae*. 
| Authors                  | Positive | Sample size | Prevalence | Country     | Study design | Type of patient         | Ward                | Site of sample | Genes                  |
|-------------------------|----------|-------------|------------|-------------|--------------|-------------------------|---------------------|----------------|------------------------|
| Akturk H, 2016 [30]     | 85       | 2805        | 0.03       | Turkey      | Case-control | Admitted               | NICU & PICU         | Rectal swab    | OXA-181, KPC-2, VIM-1, NDM-5 |
| Al Fadhi, 2020 [21]     | 7        | 590         | 0.01       | Kuwait      | Cohort       | Admitted + community    | M/S ICU (adult)     | Rectal swab    | OXA-181, KPC-2, VIM-1, NDM-5, NDM-1 |
| Antony S, 2018 [34]     | 1        | 154         | 0.01       | India       | Cross-sectional | Community              | Rectal swab         | Rectal swab    | NDM-1                   |
| Atterby C, 2018 [35]    | 2        | 307         | 0.01       | Cambodia    | Cross-sectional | Community community   | Rectal swab         | Rectal swab    | OXA-48                   |
| Baraniak A, 2015 [22]   | 110      | 17945       | 0.01       | Europe & Israel | Cohort       | Admitted               | ICU, RU             | Rectal swab    | KPC, KPC-2, KPC-3       |
| Barbadoro P, 2021 [31]  | 45       | 2478        | 0.02       | Italy       | Case-control | On Admission           | Rectal swab         | Rectal swab    | KPC, VIM                |
| Dubby BD, 2012[23]      | 21       | 299         | 0.07       | Israel      | Cohort       | On admission           | ICU                 | Rectal swab    |                        |
| Errico G, 2019 [24]     | 58       | 680         | 0.09       | Italy       | Cohort       | Admitted               | Transplant          | Rectal swab    | KPC                     |
| Ghaiith MD, 2019[39]    | 19       | 100         | 0.19       | Egypt       | Cross-sectional | Admitted               | ICU                 | Rectal swab    | NDM-1, VIM, OXA-48, OXA-181, KPC-2, VIM-1, NDM-5, NDM-1 |
| Giannella M, 2015 [26]  | 11       | 237         | 0.05       | Italy       | Cohort       | On admission           | Transplant          | Rectal swab    |                        |
| Giannella M, 2019[25]   | 38       | 553         | 0.07       | Italy       | Cohort       | On admission           | Transplant          | Rectal swab    |                        |
| Girlich D, 2014[54]     | 7        | 77          | 0.09       | Morocco     | Cross-sectional | Admitted               | Rectal swab         | Rectal swab    | OXA-48                   |
| Kang JS, 2019[32]       | 16       | 833         | 0.02       | Korea       | Case control  | On admission           | EICU                | Rectal swab    | KPC                     |
| Kiddee A, 2018[27]      | 9        | 275         | 0.03       | Thailand    | Cohort       | On admission           | ICU                 | Rectal swab    | NDM-1                   |
| Kizilates F, 2020[55]   | 11       | 168         | 0.07       | Turkey      | Cross-sectional | On admission           | Rectal swab         | Rectal swab    | OXA-48, NDM-1, VIM-1, NDM-5 |
| Liu Q, 2019[56]         | 42       | 704         | 0.06       | China       | Cross-sectional | On admission           | ICU                 | Rectal swab    | KPC, NDM, IMP          |
| Mammina C,2013[28]      | 31       | 391         | 0.08       | Italy       | Cohort       | On admission           | ICU                 | Rectal swab    | KPC                     |
| Maseda, 2017[40]        | 41       | 254         | 0.16       | Spain       | Cross-sectional | On admission           | SICU                | Rectal swab    | OXA-48                   |
| Mohan B, 2017[57]       | 9        | 232         | 0.04       | India       | Cross-sectional | Admitted               | Fecal sample        | NDN-1, VIM     |                        |
Prevalence of carbapenem-resistant *K. pneumoniae* colonization

As shown in Sheet 1, most of the studies were conducted on admission to hospital with exception of two studies from India [34] and Cambodia [35], which are conducted at community surveillance. From those who were admitted to the hospital majority of the studies have included patients admitted to ICU (14 studies), three studies on transplant recipients [24–26], and one study on patients admitted to long-term care facilities [36]. The highest prevalence was reported from India (12/54, 22%) [37], China (42/202, 21%) [38], Egypt (19/100, 19%) [39], Spain (41/254, 16%) [40] and USA (46/301, 15%) [36]. The lowest prevalence was reported from Japan (2/1467, 0.13%) [41].

The prevalence of colonization on average was 5.43% (3.73-7.42), I2= 97.87% (Figure 3). No significant change was observed in the degree of heterogeneity after excluding the known outliers and performing subgroup analysis (Table 2) and sensitivity testing.
based on the continent, study design, patient type, and admission ward. The predictive interval for the true prevalence of colonization is in a range of 3% -9% (Figure 4).

| Grouping variable | Continent | Prevalence | I-squared | Number of studies |
|-------------------|-----------|------------|-----------|------------------|
| Continent         | Asia      | 4.56(2.51-7.15) | 97.2      | 14               |
|                   | Africa    | 14.34(9.48-19.97) | 69.44    | 2                |
|                   | Europe    | 6.16(3.30-9.80) | 95.56     | 9                |
|                   | America   | 7.39 (2.34-14.84) | 92.71    | 3                |
| Design            | Cohort    | 4.98(2.07-9.02) | 97.77     | 10               |
|                   | Case-control | 2.66(1.7-3.81) | 82.01     | 4                |
|                   | Cross-sectional | 6.52(3.67-10.09) | 97.38    | 16               |

| Grouping variable | Continent | Incidence | I-squared | Number of studies |
|-------------------|-----------|-----------|-----------|------------------|
| Continent         | Asia      | 9.8(5.17-14.44) | 94.77     | 5                |
|                   | Europe    | 37.5(14.18-60.82) | 99.15     | 4                |
| Design            | Cohort    | 25(23-27.1) | 97.69     | 7                |
|                   | Cross-sectional | 59.3(53-65.2) | 98.48    | 2                |
| Ward              | ICU       | 24.6(12.37-36.83) | 99.36    | 5                |
|                   | Transplant | 17.03(14.42-19.64) |         | 2                |

The year of study, design, continent, and sample size was not statistically significant on the univariate meta-regression analysis.

**Incidence of carbapenem resistant *K. pneumoniae* colonization**

Most of the studies have assessed the incidence of CRKP colonization after admission to ICU except for three studies (two transplant units and one long-term care unit). Five of the published studies are from Asia [21, 23, 27, 32, 42], four from Europe [25, 26, 43, 44], and one from Africa [45]. The highest incidence rate was reported by studies from Greece (164/226, 0.73% and 226/498, 0.45%) and Israel (48/180, 0.27%), and the lowest incidence from Korea (16/810, 0.02%), Kuwait (22/590, 0.04%) and Thailand (13/206, 0.06%). The length of admission ranges from <8 days to 25 days from published studies.

The incidence of colonization on average was 22.3% (CI: 12.74-31.87) (Figure 5). There was still high heterogeneity after performing subgroup analysis and sensitivity testing based on the continent, admission ward, and patient type and excluding the known outliers.
After a univariate meta-regression analysis, the year of study, continent, admission ward, study design, and the sample size were not statistically significant. The 95% predictive value of the true incidence rate of carbapenem-resistant \textit{K. pneumoniae} colonization in the population ranges from 13–36\% (Figure 6).

**Drug resistance genes**

Twenty-two studies have reported the drug resistance genes, including KPC 2, KPC 3, VIM-1, IMP-4, NDM-1, NDM-5, OXA-48, and OXA-181; and KPC was the most commonly reported gene for carbapenemase production (Figure 7). OXA-48 is the typical variant of OXA, which has been reported from six studies, while OXA-181 is reported only from Kuwait.

KPC is the only class of gene variants reported from America and NDM variants are commonly reported from Asia. Though Africa is represented by two studies, KPC and IMP were not reported (Table 4).

| Continent | Genes                                      |
|-----------|--------------------------------------------|
| Asia      | OXA-181 (10), KPC-2 (98), NDM-5 (9), OXA-48 (13), NDM-1 (23), KPC (48), VIM (14), NDM (12), IMP (17) |
| Europe    | KPC-2 (91), OXA-48 (33), KPC-3 (26), KPC (136), VIM (1) |
| Africa    | OXA-48 (36), NDM-1(25), VIM (14)            |
| America   | KPC-2 (16), KPC-3 (30)                      |

**Publication bias**

Funnel plots of the standard error with proportion supplemented by statistical tests confirmed that there is some evidence of publication bias on studies reporting the prevalence of colonization with carbapenem-resistant \textit{K. pneumoniae} (Egger’s test, $p=0.0027$) and for incidence of colonization ($p=0.017$) (Figure 8).

**Discussion**

This analysis included 35 original studies addressing colonization with carbapenem-resistant \textit{K. pneumoniae}. This is the first report, to the best of our knowledge, on the global frequency of human colonization with carbapenem-resistant \textit{K. pneumoniae}. This report also details the occurrence of resistance genes in different geographic locations. Studies show that colonization with carbapenem-resistant \textit{K. pneumoniae} is increasing from 2010 until now. This review evaluates 37,661 patients from 18 countries between 2010 and 2021.

The pooled prevalence of colonization with carbapenem-resistant \textit{K. pneumoniae} is 5.43\%. This finding indicates that a significant portion of the population is colonized with CRKP, which is an indication of a huge burden as colonization could be a risk factor for infection, and one in third of people infected with CRKP will die[46]. The studies show that most of the colonization is from the Asian continent, mainly in China and India with a frequency of 1.4\%. The frequency of carbapenem-resistant \textit{K. pneumoniae} colonization in Europe was 1.2\%, 0.3\% in the Americas, and 0.07\% in Africa. Only two studies have reported colonization with carbapenem-resistant \textit{K. pneumoniae} in Africa, from Egypt and Morocco. This picture may not represent the practical scenario as most countries, especially from Africa and America have no data on colonization with CRKP.

Though higher prevalence is reported from China and India, there is still variation within those countries’ reports. In China, the prevalence report ranges from 1\%[47] to 21\% [38], and also in India, it ranges from 1\% [34] to 22\% [37]. The pooled prevalence of colonization for the Asian continent is 4.56\%. Similarly, reports from Italy show variation in the prevalence rate from 2%-9\% [24, 31] with a 6.16\% pooled estimate of prevalence for Europe. This indicates that there is no uniform distribution of colonization in different localities, even within a country.

The metaregression analysis on the type of admission ward has not shown any difference on colonization likewise with continents, sample size, and study design. The $I^2$ statistics showed a high heterogeneity even after subgroup analysis and sensitivity testing,
but the prediction interval was relatively narrow (4%-7%).

This finding indicates a significant threat posed by the pathogen as colonized peoples will serve as a source of infection for themselves and others, and people infected with CRKP have a higher healthcare cost and mortality [48, 49].

The incidence of CRKP colonization was reported from 3643 admitted patients and most of the studies included patients admitted to ICU. European countries have reported a high incidence rate (14.03%), 3.2% in Asian countries, and 0.14% in Africa. Africa is represented only by South Africa, and Europe is represented by Greece and Italy for the incidence of CRKP colonization. The pooled estimate of colonization incidence is 22.3%, with significant variation between continents (9.8% for Asia and 37.5% for European countries).

This indicates that the risk of colonization is higher in institutional and healthcare settings than in communities where such pathogenic bacteria will have been derived from patients and have continual exposure to last-resort drugs. The reality on the ground could be significantly higher than this as the data is generated only from a limited number of studies and few countries. Though the role of carriage screening indifferent setting has not been properly explored yet it may have a particularly important role in closely monitoring high-risk groups. Screening can help in setting up preventive interventions, such as decolonization and decontamination, and inform empirical treatment to minimize the risk of invasive infections[50]. Such potential interventions have to be interpreted in the light of a recent review of the interventions to control neonatal healthcare-associated infection outbreaks, indicating that enhanced swab-based surveillance was not effective at reducing case-fatality or outbreak duration[51].

The most common type of carbapenemase-producing gene bla\textsubscript{KPC} was reported from all continents except Africa, and only bla\textsubscript{KPC} were reported from the Americas. Of bla\textsubscript{KPC} variants, blaKPC-2 was the commonest type. Other genes like blaVIM, blaOXA-like, and blalMP, were reported from other continents. The most common variant of blaOXA-like was blaOXA-48 which was reported in most parts, but one variant blaOXA-181, was reported only from Kuwait. European countries have not reported blaNDM variants though these variants were commonly reported from Asian countries. This finding is in line with [52, 53] where they have indicated blaNDM-1 was the commonest variant and reported commonly from India and China.

Heterogeneity across studies represents an important limitation in combining observational studies for meta-analysis. We attempted to limit this heterogeneity through the use of relatively narrow inclusion criteria and assessing the quality of included studies via a JBI protocol. For the identified heterogeneity, we use meta-regression to explain potential sources of heterogeneity. Although a large number of patients were included in the studies, the small number of included studies limited the power to assess for publication bias.

The strength of this review lies in its adherence to established methods for conducting systematic reviews, extensive searching, an inclusive date range, and combined quality assessment of the included studies. Compiling all available evidence on this matter will help Healthcare settings to take an informed decision for screening and segregating colonization, organizations working on human health to devise strategies in the decolonization of colonized peoples as well as design a strategy to reduce colonization with this resistant pathogen.

## Conclusion And Recommendations

In conclusion, this review details the prevalence and incidence of colonization with carbapenem resistant \textit{K. pneumoniae} and drug resistance genes. Most of the studies are from developed countries and from healthcare stings, leaving under developed countries as well as community members unrepresented by this review. Studies have reported a variable distribution of colonization with \textit{K. pneumoniae} from different areas ranging from 0.13% to 22% for prevalence in the community or at admission into setup while for incidence colonization ranges from 2% to 73% with a pooled prevalence of 5.43% and incidence of 22.3%. The incidence rate is relatively higher than prevalence depicting that colonization is higher in healthcare settings than in the community. There was a significant heterogeneity on both prevalence and incidence pooled estimates with $I^2$ statistics, yet, the predictive value for the prevalence is narrow.

On the other hand, various drug resistance genes have been reported from colonizing strains, and the commonest type of resistance gene is KPC, and NDM genes were reported to form Asian countries mainly. All in all, resistance genes have variable
distribution across geography.

As most of the reports are from healthcare settings and in developed countries, there is no clear picture of the problem in the community and the developing world. Thus, we recommend more studies from developing parts of the world and from the community setting. In general, this review has detailed a higher presence of colonizing \textit{K. pneumoniae} which alarms for devising a strategy for decolonization.

**Abbreviations**

CRE- Carbapenemase Producing Enterbacterales

CRKP- Carbapenemase producing \textit{Klebsiella pneumoniae}

ESBL- Extended Spectrum \(\beta\)-Lactamase

GIT- Gastrointestinal Tract

ICU- Intensive Care Unit

JBI- Joanna Briggs Institute

MBL- Metallo-\(\beta\)-lactamase

OMP- Outer Membrane Protein

PCR- Polymerase Chain Reaction

PRISMA- Preferred Reporting Items for Systematic Reviews and Meta-Analyses

USA- United States of America

**Declarations**

**Availability of Data and Materials**

All data generated or analyzed during this study are included in this published article as supplementary information files.

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**Author’s Contributions**

TT and NA conceived and designed the study. NA, HM and ME had participated in collecting scientific literature, critical appraisal of articles for inclusion, analysis, and interpretation of the findings. TT drafted the manuscript and prepared the manuscript for publication. All authors have read and approved the final version of the manuscript.

**Ethics declarations**

**Ethics approval and consent to participate**

Not applicable.
Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

PRISMA flow chart of articles screened for colonization of carbapenem-resistant K. pneumoniae
Figure 2

Distribution of studies reporting colonization with carbapenem-resistant *K. pneumoniae* in different continents

Figure 3

Forest plot for prevalence of Carbapenem-resistant *K. pneumoniae* colonization
Distribution of True Effects for prevalence

The true effect size in 95% of all comparable populations falls in the interval 0.03 to 0.09

Figure 4
Predictive interval for population prevalence of Carbapenem-resistant *K. pneumoniae*
| Study                    | ES (95% CI)     | Weight |
|-------------------------|-----------------|--------|
| Al Fadhi, 2020          | 3.73 (2.48, 5.58) | 10.36  |
| Chueansuwan 2016        | 18.75 (12.20, 27.70) | 7.72   |
| Dubby BD, 2012          | 26.67 (20.74, 33.54) | 9.28   |
| Giannella M, 2015       | 12.86 (9.01, 17.50) | 10.18  |
| Giannella M, 2019       | 19.71 (16.61, 23.32) | 0.26   |
| Kang JS, 2019           | 1.98 (1.22, 3.18)  | 10.36  |
| Kishke A, 2016          | 23.76 (16.56, 31.50) | 10.28  |

**Figure 5**

Forest plot for incidence of Carbapenem-resistant *K. pneumoniae* colonization
The true effect size in 95% of all comparable populations falls in the interval 0.13 to 0.38.

**Figure 6**

Predictive interval for population incidence of Carbapenem-resistant *K. pneumoniae*
Figure 7
Distribution of carbapenem-resistance genes among colonizing *K. pneumoniae* isolates from different studies

Figure 8
Funnel plot depicting publication bias among studies for prevalence of carbapenem-resistant *K. pneumoniae* colonization

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

- ExtractedDataColonization.xlsx
- RecordAppraisal.docx