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THE GLOBAL EMERGENCE OF VENTILATOR-ASSOCIATED PNEUMONIA (VAP) IN THE ERA OF THE COVID-19 PANDEMIC: A DESCRIPTIVE STUDY

Larion JJ[1] and Pai C[2*]

[1]*Touro University College of Osteopathic Medicine, California, USA*
[2]*Foundational Biomedical Sciences Dept., Touro University College of Osteopathic Medicine, California, USA*

Abstract: Ventilator-associated pneumonia has been a well-known complication in the intensive care unit (ICU) and continues to be a real threat in patients infected with coronavirus disease (COVID- 19), particularly in those that progress to acute respiratory distress syndrome (ARDS) with subsequent mechanical ventilation. Through a global perspective, this descriptive study was aimed at describing the patterns of co-infection with ventilator-associated pneumonia (VAP) in patients with COVID-19 ARDS. The global incidence rate of VAP in COVID-19 patients on mechanical ventilation was determined to be 41.2% supported by extended time spent on mechanical ventilation, increase in mortality rate, and the emergence of drug-resistant microbes. These outcomes are accompanied by the concomitant presence of previous antimicrobial use, invasive respiratory operations due to COVID-19 ARDS, and in some cases, corticosteroid treatment. The results of our findings add to the emergent threat of VAP as an important nosocomial infection as the COVID-19 pandemic persists.

Keywords: Ventilator Associated Pneumonia (VAP), COVID-19, ARDS, Multidrug resistant microbes

Introduction

Patients in the intensive care unit (ICU) have increased mortality risk from critical illness and secondary processes, such as nosocomial infections. Hospital-acquired pneumonia is the most common nosocomial infection in critically ill patients and thirty-two percent of which are associated with mechanical ventilation and are termed ventilator-associated pneumonia (VAP). (National Healthcare Safety Network, 2022). The pandemic of coronavirus disease (COVID-19) has led to the critical need for tracheal intubation and mechanical ventilation of large numbers of patients admitted to intensive care units (ICUs). VAP has been noticed as a common complication in these patients with unfavorable outcomes including high morbidity and mortality.

The pathophysiology of COVID-19 among critically ill and mechanically ventilated patients involves an aggressive release of inflammatory cytokines that result in diffuse alveolar damage and acute respiratory distress syndrome (ARDS). (Ragab et al., 2020). Patients who have reached this point of severity in the disease course often require respiratory support via mechanical ventilation and for

*Corresponding Authors' Email: cpai@touro.edu

overall longer periods than non-COVID ARDS. (Aslan et al., 2021). Extended time spent on mechanical ventilation increases the risk of VAP onset, which is defined by at least forty-eight consecutive hours on mechanical ventilation, the presence of a new or progressive radiographic infiltrate, plus at least two of three clinical features (fever greater than 38°C, leukocytosis or leukopenia, and purulent secretions). (American Thoracic Society, & Infectious Diseases Society of America, 2005). Furthermore, there are shared characteristics in patient profile and patient management by COVID-19 patients and patients who develop VAP which include elderly age, male gender, presence of comorbid disease, smoking history, invasive respiratory operations, and previous antimicrobial use. (Wu et al., 2019; Gao et al., 2021).

Several factors including extrinsic and intrinsic ones are responsible for increased incidence of VAP in critically ill COVID patients compared to non-COVID patients. The extrinsic factors include understaffing, lack of personal protective equipment and use of immunomodulating agents such as corticosteroids, interleukin-6 (IL-6) antagonists and Janus Kinase inhibitors. The intrinsic factors that contribute to increased incidence of VAP are severe parenchymal damage and immune dysregulation, along with pulmonary vascular endothelial inflammation and thrombosis. (Boyd et al.,2022).

From a management perspective, several good preventive measures have been studied including elevation of the head of the bed, draining of subglottic secretions, maintenance of endotracheal cuff pressure etc., to decrease the risk of aspiration in all intubated patients. (Isac et al., 2021). Different techniques such as regular tooth brushing and chlorhexidine mouthwash have also been shown to decrease rates of VAP. Conversely, routine circuit changes have been shown to increase rates of VAP. (Han et al., 2010)

The aim of the research project was to carry out a systematic review of the VAP cases reported in COVID-19 patients admitted to ICUs. The main objectives of the review included,

- Exploring and searching databases including PubMed, EMBASE, and ScienceDirect for global reports of COVID-19 associated VAPs.
- Reviewing data published in 2019, 2020, 2021 and early 2022 and comparing the global incidence of VAP in COVID-19 patients.
- Analyzing the reported risk factors and the presence of co-morbidities in COVID-19 patients developing VAP.
- Studying the spectrum of etiologic agents including bacteria and fungi and enumerating the most common pathogens involved in these infections.
- Discussing the preventative aspects that can help lower the incidence of VAP in intubated COVID-19 patients.

Materials and Methods

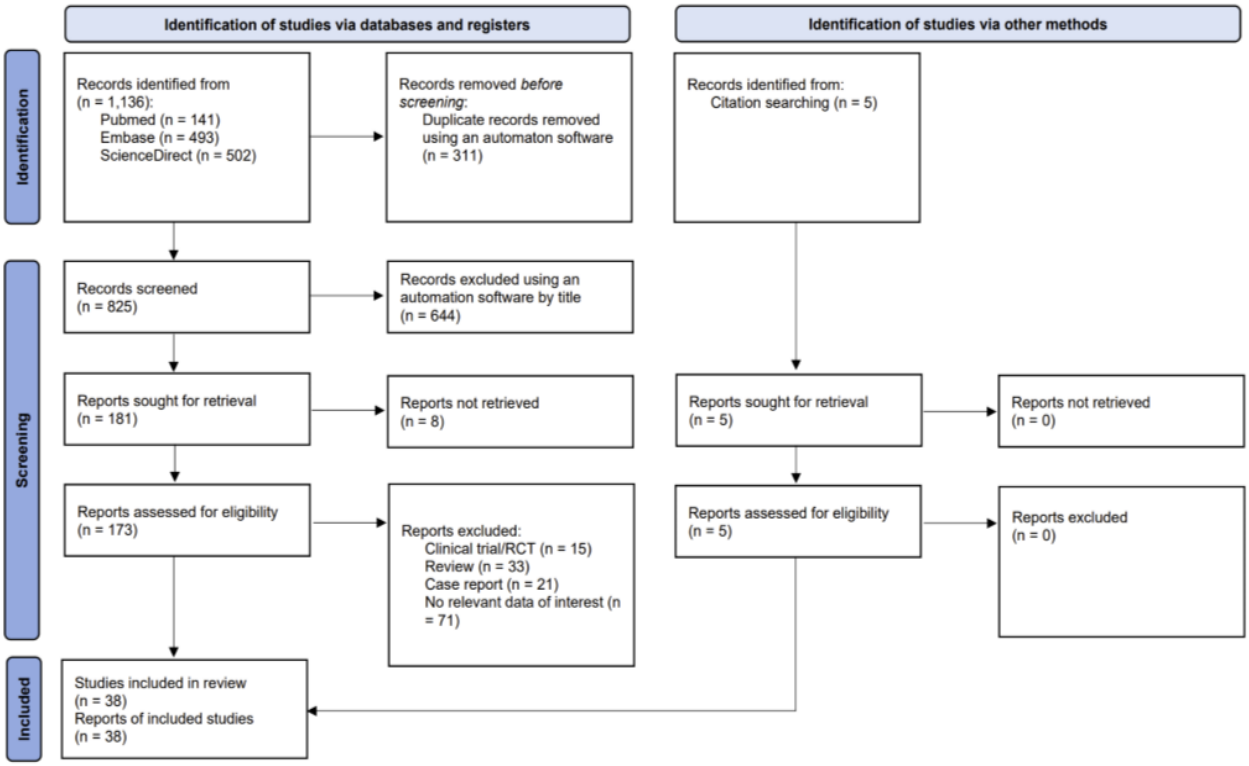

Figure 1: PRISMA flow diagram for new systematic reviews which included searches of databases, registers, and other sources. (Page et al., 2021).

Figure 1 highlights the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) methodology used for the collection of references collected over a 12-week period from 9 Nov 2021 to 9 February 2022. A structured literature review was conducted using Medline (PubMed), Embase, and ScienceDirect. Combinations of the key search terms “ventilator-associated pneumonia,” “VAP,” “coronavirus,” “COVID-19,” and “SARS-CoV-2" were used for obtaining a comprehensive list of articles within publication dates filtered from Dec 2019 to Feb 2022. The search terms helped select the relevant articles for a comprehensive understanding of the incidence of Ventilator Associated Pneumonias (VAP) in patients with COVID infection. The Sciwheel© citation manager was utilized as an automation tool to eliminate duplicate reports among the specified databases. After duplicates were removed, further filtering by title and abstracts were assessed as a preemptive screen to rule out unrelated articles. An exclusion criterion was developed and applied if articles were categorized as clinical trials/randomized control trials, literature reviews, case reports, and no valuable and/or relevant data pertaining to this study. Cross references of select articles were also referred and added to the total number of articles included in this study.

Results and Discussions

Although the publication years included Dec 2019 to February 2023, we noted that most of the publications involved research data obtained during 2020 and 2021. Hence, we thought it appropriate to compare the characteristics of data obtained from these two study years. We opine that as the pandemic was just beginning in late 2019 and was waning by early 2023, the incidences of COVID-19 with VAP peaked during 2020 and 2021.

Table 1. Characteristics of 38 studies. Categorized by study period (2020 and 2021) alphanumerically sorted by country and includes data regarding mechanically ventilated COVID-19 patients, management, and outcomes.

VAP – Ventilator-associated Pneumonia; MV – Mechanical Ventilation

2020 Study Period									
Author	Country	Sample size	Male Gender	Median Age	# Of COVID-19 on MV	Median Duration on MV	VAP positive [n (%)]	# Of Isolated Microbes from VAP	Deceased with VAP
Moretti, et. al., 2021	Belgium	39	28	62	39	21	21 (53.8)	27	11
Costa, et al., 2022	Brazil	191	116	70.5	115	13	45 (39.1)	43	21
Zhou, et al., 2022	China	191	119	56	32	-	10 (31.3)	-	-
Chen, et al., 2020	China	99	67	55.5	17	17	10 (31.3)	3	-
Rojas-Fermin, et al., 2021	Dominican Republic	382	-	-	119	-	6 (5.0)	-	6
Maes, et al., 2021	England	81	56	62	81	14	39 (48.1)	118	-
Rouze, et al., 2021	France, Spain, Greece, Portugal, and Ireland	568	407	64	568	15	205 (36.1)	311	-
Reva Network COVID-ICU group, 2021	France, Belgium, and Switzerland	4244	3159	63	2635	13	1209 (45.9)	-	-
Blonz, et al., 2021	France	188	147	63.9	188	22.2	92 (48.9)	25	28
Dudoignon, et al., 2021	France	54	42	63	49	12	15 (30.6)	17	-
Ferre, et al., 2022	France	189	140	65	189	19	110 (58.2)	-	-
Gangneux, et al., 2022	France	509	400	59.4	509	27.1	374 (73.5)	-	137
Luyt, et	France	58	36	48	54	45	43 (79.6)	44	4

al., 2020									
Razazi, et al., 2020	France	90	74	59	90	16.5	56 (62.2)	72	-
Roger, et al., 2021	France	966	720	66	721	-	342 (47.4)	-	69
Rouyer, et al., 2021	France	79	55	60	79	-	42 (53.2)	50	22
Jamnani, et al., 2022	Iran	38	10	66.8	22	-	22 (100.0)	22	10
Sharifipour, et al., 2020	Iran	19	11	67.1	19	-	19 (100.0)	19	-
Baccolini, et al., 2021	Italy	41	30	72	37	9	15 (40.5)	-	-
De Santis, et al., 2022	Italy	248	193	66	248	-	62 (25.0)	-	-
Gamberini, et al., 2020	Italy	391	300	66	391	16	251 (64.2)	-	-
Giacobbe, et al., 2021	Italy	568	137	64	586	-	171 (29.2)	96	77
Grasselli, et al., 2021	Italy	774	597	62	689	14	389 (56.5)	389	82
Castaneda-Mendez, 2021	Mexico	61	-	-	61	-	32 (52.5)	45	-
Bardi, et al., 2021	Spain	134	108	61	134	-	21 (15.7)	21	-
Suarez-de-la-Rica, et al., 2021	Spain	107	76	62.2	107	-	35 (32.7)	35	29
Søgaard, et al., 2021	Switzerland	34	99	64.4	34	-	5 (14.7)	4	-
Weinberger, et al., 2022	USA	661	423	60	628	11	94 (15.0)	-	52
Pickens, et al., 2021	USA	179	110	62.4	179	13	72 (40.2)	41	3

Papamanoli, et al., 2020	USA	469	303	61	172	-	48 (27.9)	65	-
Bolker, et al., 2022	USA	228	128	68	72	-	45 (62.5)	-	-
Risa, et al., 2021	USA	126	88	59	126	-	69 (54.8)	113	-
Bychinin, et al., 2022	Russia	168	81	64	111	-	75 (67.6)	98	47
Ong, et al., 2021	Singapore	27	59	52	27	-	1 (3.7)	-	-

2021 Study Period

Author	Country	Sample size	Male Gender	Median Age	# Of COVID-19 on MV	Median Duration on MV	VAP positive [n (%)]	# Of Isolated Microbes from VAP	Deceased with VAP
Meawed, et al., 2021	Egypt	197	118	65	197	-	197 (100.0)	331	197
Luque-Paz, et al., 2022	France	178	135	67	178	14.5	66 (37.1)	77	-
Cohen, et al., 2021	Israel	93	65	67	93	-	64 (68.8)	70	33
Carbonell, et al., 2021	Spain, Andorra, and Ireland	3795	2686	64	2888	15	775 (26.8)	775	340

Table 1 summarizes the characteristics of the thirty-eight studies categorized by study period. Of these, 34 articles included study periods during the year 2020, while four included 2021. Articles included in this study are represented by countries of Europe (25), Asia (6), North America (6), and Africa (1). Across all studies, the total study patient population was 16,482 COVID-19 patients with a preponderance of the male gender at 71.7% based on 36 studies that included data on gender distribution. All studies focused on adult patients with a mean age of 62.7 years (across an age range of 21 to 92 years old).

Comparative incidence rates of VAP in patients with COVID-19 on intubation:

The global incidence rate of ventilator-associated pneumonia was determined to be 41.2% based on our evaluation of the 38 studies. However, it is noteworthy that most reports on the incidence of VAP in intubated COVID-19 patients came from France and Italy in Europe, the highest incidences reported being 79.6% from France (Luyt et al., 2020) and 64.2% from Italy (Gamberini et al., 2020). Incidences reported from the US ranged between 15% (Weinberger et al., 2022) to 62.5% (Bolker et al., 2022). High incidences of 100%, 68.8% and 67.6% were reported from Iran and Egypt; Israel and Russia respectively.

Extrapolating from findings, three studies (two from Iran and one from Egypt) demonstrated a 100% incidence rate of VAP in mechanically ventilated COVID-19 patients and 12 other studies demonstrated an incidence rate greater than 50%. These findings do reflect the extent to which these countries reeled under the impact of the waxing and waning pattern of the COVID-19 pandemic in which a second wave transitioned to a third wave between July 2020 into early 2021. In a study conducted in Iran, a decrease in the quality of care due a combination of factors, such as high workload, nurse staffing shortages, and high rate of used equipment during this stage of the pandemic may also explain the increased incidence rates of VAP. (Sharifipour et al., 2020).

Association of COVID-19 and VAP with comorbidities:

Table 2: Prevalence of comorbid disease among 15,169 COVID-19 patients across 30 studies.

Comorbid Disease	n (%)
Hypertension	6733 (44.4)
Diabetes	4039 (26.6)
Obesity	3307 (21.8)
Respiratory Disease	1120 (7.4)
Heart Disease	1103 (7.3)
Immunodeficiency	734 (4.8)
Neurological Disorder	616 (4.1)
Corticosteroid Use	472 (3.1)
Blood Disorder	447 (2.9)
Smoking	399 (2.6)
Dyslipidemia	344 (2.3)
CKD	339 (2.2)
Cancer	193 (1.3)
Other Endocrine Disorder	64 (0.4)
Solid Organ Transplant	53 (0.3)
Liver Disease	51 (0.3)
OSA	38 (0.3)
GI Dysfunction	11 (0.1)

30 studies included patient information pertaining to the presence of comorbid disease [Table 2]. Hypertension was predominant across all patients (44.4%), followed by diabetes mellitus (26.6%),

obesity(21.8%), respiratory disease (7.4%), heart disease (7.3%), immunodeficiency (4.8%), neurological disorder (4.1%), corticosteroid use (3.1%), non-malignant blood disorders (2.9%), smoking history (2.6%), dyslipidemia (2.3%), chronic kidney disease (2.2%), cancer (1.3%), and less than one percent each of other comorbid diseases.

For the purposes of this study, we only considered patients specified as both COVID-19 positive and on mechanical ventilation for further evaluation (n =12,484). From the excluded study populations, COVID-19 positive but not requiring mechanical ventilation (n = 3,982) and non-COVID ARDS (n = 16) were reasons for exclusion. From the newly defined population, the mean time (days) spent on mechanical ventilation was 17.2 days. The clinical definitions used to determine VAP were conserved among the 38 studies. Of the 12,484 COVID-19 positive patients on mechanical ventilation, 5,147 (41.2%) were positive for VAP with a mean time (days) spent on mechanical ventilation of 8.9 days before a first episode of VAP. 71 patients across four studies were documented to experience more than one episode of VAP. Of these, one study mentions 11 patients with four recurrent episodes of VAP. 18 studies included data on mortality rates in VAP positive patients. From these, a 40.7% mortality rate was observed. The other 59.3% had either recovered or not stated to be deceased with VAP during the study period.

Thus appropriate management of comorbidities such as hypertension, diabetes and obesity are important measures that can reduce the VAP related mortality in COVID-19 patients that require intubation.

Correlation of pathogen types status isolated from COVID-19 patients with VAP.

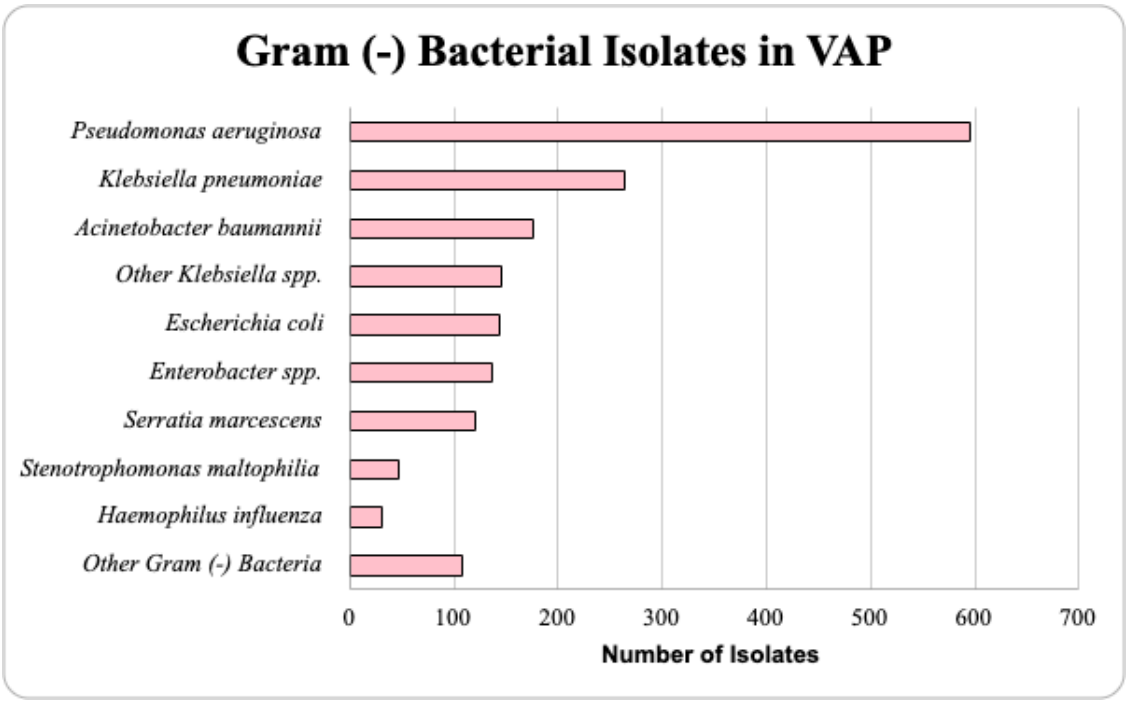

Figure 2. Total number of Gram-negative bacterial isolates from VAP positive patients (n = 1752)

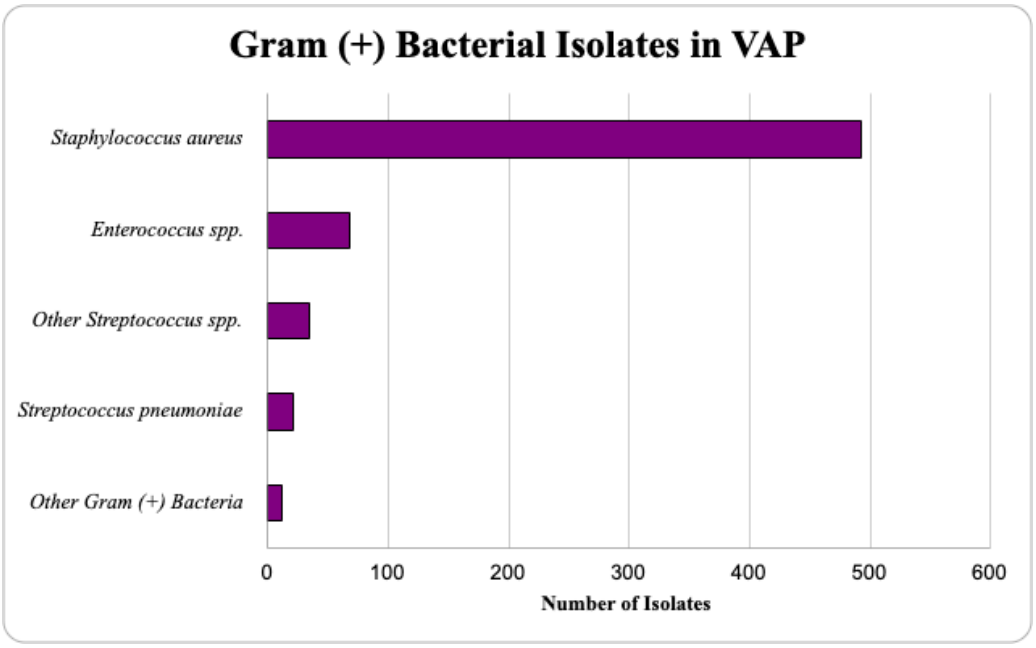

Figure 3. Total number of Gram-positive bacterial isolates from VAP positive patients (n = 568).

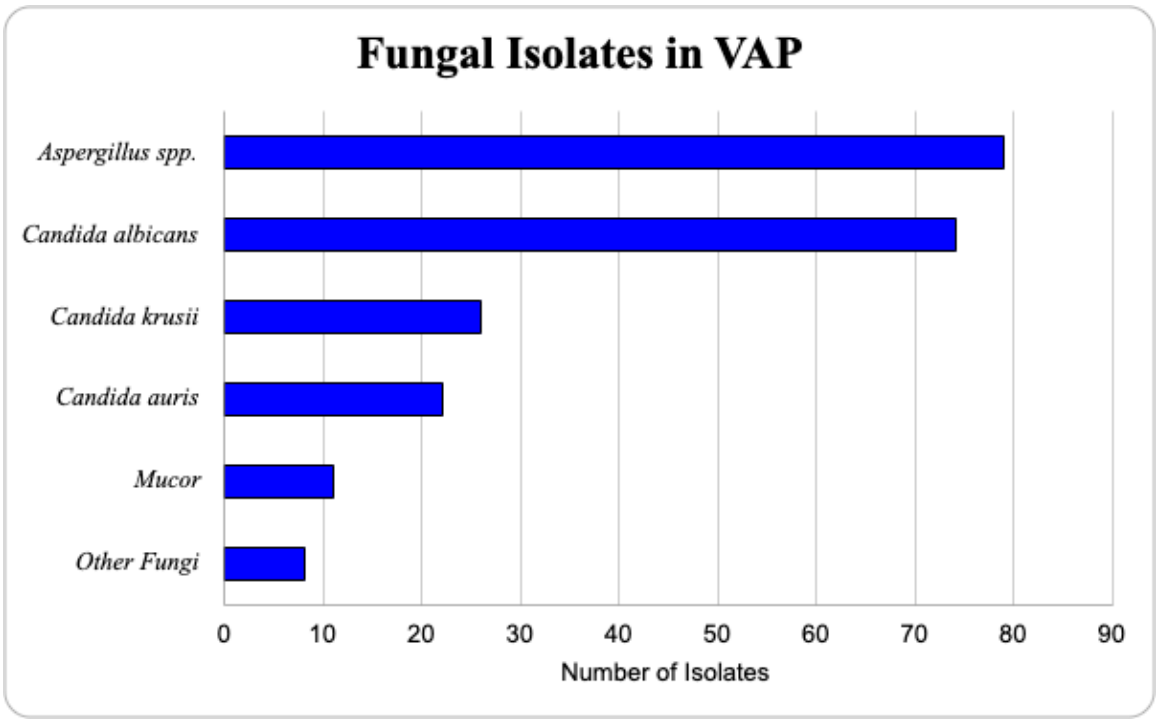

Figure 4. Total number of fungal isolates from VAP positive patients (n = 211).

Status of antimicrobial resistance amongst the various isolates obtained from COVID-19 patients with VAP

Figure 5. Antibiotic susceptibility of 2,545 bacterial isolates from 20 studies; a) represents the percentage of all bacterial isolates from VAP as drug-resistant or -susceptible; b) represents the percentage of resistant bacterial isolates of VAP. [MDR – Multidrug Resistant; MRSA – Methicillin-resistant Staphylococcus aureus; PDR – Pan-Drug Resistant; ESBL – Extended Spectrum β-Lactamase]

Further, we studied the microbial etiology and antibiotic susceptibility profiles of the microbial isolates from 26 studies that gave detailed characterization of etiologic microbes causing VAP totaling 2,911 isolates. Among these, 1752 (60.2%) were Gram-negative bacteria, 568 (19.5%) were Gram-positive bacteria, 211 (7.2%) were fungal, and 380 (13.1%) were other unspecified microbes. From the Gram-negative bacterial isolates, 600 (34.2%) were *Pseudomonas aeruginosa*, 408 (23.3%) were *Klebsiella* spp. (including 267 *Klebsiella pneumoniae*), 172 (9.8%) were *Acinetobacter baumannii*, 141 (8.0%) were *Escherichia coli*, 139 (7.9%) were *Enterobacter* spp., and 138 (7.9%) were *Serratia marcescens* isolates. [Figure 2]. Gram-positive bacterial isolates included 454 (79.9%) *Staphylococcus aureus* (Methicillin-susceptible and methicillin–resistant species), 49 (8.6%) *Enterococcus* spp., *Streptococcus* spp., 56 (9.8%) and *Streptococcus pneumoniae*, 36 (5.9%), and less than one percent each of other Gram-positive bacteria [Figure 3]. Fungal isolates were represented by *Candida* spp. (121; 57.3%), *Aspergillus* spp. (79; 37.4%), and *Mucor* (11; 5.2%) [Figure 4]. An exhaustive list of bacterial and fungal isolates is available in the appendices Table S1.

With respect to etiologic microbes of VAP, the most common bacterial isolates of VAP before the pandemic were *Staphylococcus aureus* (28.4 %), *Pseudomonas aeruginosa* (25.2 %), and other gram negatives (26.6%), including *Klebsiella* spp. and *Enterobacter* spp. due to the likelihood of colonization on artificial airways. (Kohbodi et al., 2022). Similarly, *Pseudomonas aeruginosa* (20.6%) and *Staphylococcus aureus* (15.6%) were predominant across all isolated microbes in VAP patients during the pandemic. Polymicrobial VAP was documented in 142/537 (26%) patients across seven studies. From these, one study noted statistical significance ($p < 0.005$) in the correlation between elderly age, pretreatment by antimicrobials, and longer durations on mechanical ventilation with the onset of polymicrobial VAP. (Blonz et al., 2021).

Typically, fungal infections are reserved for periods of being immunocompromised. In a study conducted in Egypt, fungal causes of VAP were prevalent (134/197; 68%) and showed a statistically significant relationship between VAP onset and presence of diabetes (95% confidence interval [CI]

1.09−3.31; p = 0.02), hyperthyroidism (95% CI 1.01−4.78; p = 0.05), and longer durations of mechanical ventilation (p < 0.001); additionally, all patients with fungal VAP were under treatment by corticosteroids and Tocilizumab prior to the onset of pneumonia. Underreporting of fungal isolates may have occurred in this study due to variances in systemic screening. However, we did note a strong presence of fungal VAP in their study population (134/197; 68.0%) which included fungi such as *Candida albicans, C. krusei, C. auris, Aspergillus* spp., and *Mucor.* (Maewed et al., 2021). Other studies described the threat of COVID-associated fungal infections including COVID-19-associated pulmonary aspergillosis (CAPA), COVID-19-associated mucormycosis (CAM), emergence of *Candida auris,* and invasive candidiasis which are still underreported in this present time. (Kundu et al., 2022).

Thus, the current trends in the etiological agents shows a tilt in the balance towards gram negative bacterial pathogens many of which are multi or even pan drug resistant. It is important to consider these factors while coming up with empirical treatment protocols in any given region and its hospitals.

Data pertaining to antibiotic sensitivity was available from 20 of the studies which described them in detail. Presence of antibiotic resistance was observed in 630/2545 (24.8%) of bacterial isolates [Figure 5a]. Of these resistant bacteria, 321 (51.8%) were multidrug resistant (MDR), 124 (20.0%) were Methicillin-resistant Staphylococcus aureus (MRSA), 81 (13.1%) were pan-drug resistant (PDR), 79 (12.7%) were separately characterized from MDR as extended-spectrum β-lactamase-producing, 18 (2.9%) were extensive drug resistant (XDR), and 7 (1.1%) were resistant to carbapenem [Figure 5b].

Challenges involved and best practices for the prevention of COVID -19 associated VAP.

From our literature review, we observed that in addition to the burden of maintaining quality of care during the successive waves of the pandemic, practice guidelines and methods including the use of antimicrobial agents for treatment of the COVID-19 condition can easily lead to the emergence of highly drug resistant pathogens. Between the three studies that demonstrated a 100% VAP incidence rate, 227/238 (95.3%) of bacterial isolates were drug resistant. As outlined by the Infectious Disease Society of America and the American Thoracic Society, risk factors of MDR VAP include previous antimicrobial use in the preceding 90 days and ongoing ARDS. (Kalil et al., 2016). A study conducted in Egypt demonstrated 197/197 (100%) patients received empiric antibiotic treatment upon admission; of which, all patients went on to develop drug resistant VAP comprised of 81 pan-drug resistance (PDR), 54 multidrug resistance (MDR), 44 Extended Spectrum β-Lactamase (ESBL), and 18 Methicillin Resistant Staphylococcus aureus (MRSA). (Maewed et al., 2021). With MDR as the overall predominant level of resistance found among all bacterial isolates (51.8%), these findings emphasize a strict protocol required in the ICU and an adherence to the antibiotic stewardship guidelines., especially in the compromising setting of mechanical ventilation.

The outcomes of VAP further support the priority of prevention. Among 5138 COVID-19 patients with VAP across eighteen studies, 2859 (40.9%) patients were reported deceased by their respective study's endpoints. A 2011 study on the attributable mortalities due to VAP found a higher mortality rate in VAP compared to non-VAP patients at an attributable rate of 32.5%. (Agrafiotis et al., 2011).

It is noteworthy that two separate studies in the Dominican Republic and in Singapore demonstrated an overall incidence rate of VAP of less than 10% (5% and 3.7%, respectively). (Ong et al., 2021; Rojas et al., 2021). In the study conducted in Singapore, specific protocols are outlined and attributed

to the low incidence rate in their study population of 27; these include a semi-recumbent positioning during mechanical ventilation as a protective measure specifically against VAP. (Ong et al., 2021). An additional study conducted in France observed a comparatively lower incidence rate of VAP in patients who were pretreated with selective digestive decontamination as a prophylactic strategy versus not (21% vs 50%, respectively). (Luque-Paz et al., 2022).

Increased ventilation time is a secondary, less severe outcome of VAP. Six studies included data concerning the median ventilation time of all COVID-19 patients and COVID-19 patients who went on to develop VAP. On average, COVID-19 patients with VAP remained on mechanical ventilation for longer durations (21.5 days vs. 14 days). In addition to the staff required to support extended management of VAP patients, there is an increased financial burden to the hospital, patients, and families. As reported by the Infectious Disease Society of America and the American Thoracic Society in 2016, VAP increased duration on mechanical ventilation accompanied by upwards of $40,000 excess costs per patient. (Kalil et al., 2016).

Several good preventive measures have been studied including elevation of the head of the bed, draining of subglottic secretions, maintenance of endotracheal cuff pressure etc., to decrease the risk of aspiration in all intubated patients. (Isac et al., 2021). Different techniques such as regular tooth

brushing and chlorhexidine mouthwash have also been shown to decrease rates of VAP. Conversely, routine circuit changes have been shown to increase rates of VAP. (Han et al., 2010).

Conclusion

Based on our systematic review we conclude that the incidence of VAP among intubated COVID-19 patients directly correlated with the severity of the pandemic and the ability of the health care system to adhere to quality health care. Gram negative pathogens were mainly responsible for the cases of VAP and muti-drug resistance posed a major challenge. Fungal pathogens are also on the rise.

COVID-19 patients who developed VAP experienced longer mechanical ventilation durations, leading to polymicrobial infections and drug resistant microbes, recurrent episodes, and increased mortality rate. Those at risk for or with COVID-19 are also at risk for developing VAP. Important preventative measures to be considered include multiple factors such as good control of the underlying morbidity such as hypertension, diabetes and obesity; strict adherence to antibiotic stewardship protocols. Other nursing measures including elevation of the head of the bed, draining of subglottic secretions, maintenance of endotracheal cuff pressure etc., to decrease the risk of aspiration in all intubated patients as well as maintenance of good oral hygiene by regular toothbrushing and chlorhexidine mouthwashes to decrease the risk of aspiration of harmful pathogens.

Limitations of our study

This review was based on VAP cases detected among intubated patients with COVID-19 infection only. However, we did not consider analyzing VAP cases among non-COVID patients during the same time. This would have helped compare differences in the incidence rates, underlying co-morbidities as well as the spectrum of pathogens and drug resistant strains involved.

Future scope: Further review of specific preventative interventions and their impact on the incidence of VAP and patient outcomes will help us draw meaningful conclusions about the best practices involved in the prevention of COVID-19 associated VAP.

Declaration of Interest Statement

The authors declare that they have no conflict of interests.

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Appendix

Table S1: Documented Isolates from VAP patients, including Gram-negative bacteria, Gram-positive bacteria, and Fungi.

Gram-negative bacteria (*n* = 1750)		
Species	***n***	**%**
Pseudomonas aeruginosa	600	34.2%
Klebsiella pneumoniae	267	15.2%
Acinetobacter baumannii	172	9.8%
Other *Klebsiella spp.*	141	8.0%
Escherichia coli	139	7.9%
Enterobacter spp.	138	7.9%
Stenotrophomonas maltophilia	87	5.0%
Serratia marcescens	79	4.5%
Haemophilus influenza	31	1.8%
Citrobacter spp.	27	1.5%
Other *Acinetobacter spp.*	19	1.1%
Proteus mirabilis	13	0.7%
Burkholderia cepacia	8	0.5%
Other Proteus spp.	9	0.5%
Morganella morganii	5	0.3%
Hafnia spp.	5	0.3%
Enterobacter	4	0.2%

aerogenes		
Other *Serratia spp.*	3	0.2%
Comamonas kerstersii	2	0.1%
Moraxella Catarrhalis	1	0.1%
Chryseobacterium indologenes	1	0.1%
Other *Pseudomonas spp.*	1	0.1%
Gram-positive Bacteria (*n* = 568)		
Species	***n***	**%**
Staphylococcus aureus	454	79.9%
Enterococcus spp.	49	8.6%
Other *Streptococcus spp.*	36	6.3%
Streptococcus pneumoniae	20	3.5%
Other *Staphylococcus spp.*	6	1.1%
Corynebacterium accolens	1	0.2%
Corynebacterium striatum	1	0.2%
Nocardia nova	1	0.2%
Fungi (*n* = 211)		
Species	***n***	**%**
Aspergillus spp.	79	37.4%
Candida albicans	73	34.6%
Candida krusii	26	12.3%

Candida auris	18	8.5%
Mucor	11	5.2%
Candida tropicalis	2	0.9%
Candida dubliensis	1	0.5%
Candida parapsilosis	1	0.5%

Other Unspecified Microbes (*n* = 380)

Species	***n***	**%**
-	380	13.1%