Int.J.Curr.Microbiol.App.Sci (2018) *7*(4): 907-921

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 7 Number 04 (2018)**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2018.704.097

A Study of Incidence and Microbiological Profile of Ventilator Associated Tracheobronchitis (VAT) in a Tertiary Care Hospital

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Keywords

Ventilator associated tracheobronchitis, Ventilator associated pneumonia, Multi drug resistance

Article Info

Accepted:
07 March 2018
Available Online:
10 April 2018

A B S T R A C T

Ventilator-associated tracheobronchitis (VAT) is a common intensive care unit (ICU)-acquired infection. Its incidence ranges from 1.4 to 19% of critically ill patients receiving invasive mechanical ventilation. This infection is considered as an intermediate process between between colonization and ventilator-associated pneumonia (VAP). 1. To study the incidence of VAT. 2. To study the microbiological profile and anti-microbial susceptibility. This is a prospective study of 149 intubated patients. The endotracheal aspirates were collected and processed. VAT was diagnosed on microbiological and clinical basis. All the relevant clinical details were recorded. An incidence of 24.83% of VAT cases was recorded with male predominance. Various underlying conditions like Cerebrovascular accident, Coronary artery disease, Chronic kidney disease were found to be associated with VAT. Most of them had comorbidities such as hypertension and diabetes mellitus. *Acinetobacter baumannii* (33.33%), *Klebsiella pneumoniae* (22.22%), *Candida albicans* (13.33%) and *Staphylococcus aureus* (11.11%) were the most frequently encountered pathogens in patients with VAT. The mortality was found to be 18.92%. Patients with VAT experienced longer ICU stay and more prolonged mechanical ventilation compared to patients without VAT. Formulation of a good infection control policy and emphasis on health education will prevent the transmission of multidrug-resistant organisms in the Intensive care units.

Introduction

Ventilator associated respiratory infections are the most common infections in persons receiving mechanical ventilation. Ventilator associated tracheobronchitis (VAT) and Ventilator associated pneumonia (VAP) occur 48 hours after the onset of mechanical ventilation. The prevalence varies from 1.4-19% (Nseir and Martin-Loeches, 2014). Ventilator associated tracheobronchitis (VAT) is considered to be an intermediate between colonisation and ventilator associated pneumonia (Martin-Loeches and Pobo, 2010). Many definitions are available for the diagnosis of VAT but none is sensitive or specific. The most widely accepted criteria include fever, purulent tracheal secretions

moderate to heavy growth by semi quantitative method (>10^5CFU/ml and the absence of chest radiographic findings (Martin-Loeches *et al.,* 2013). The incidence of VAP is increased in patients with VAT (Craven, 2008).

VAT can be caused by both Gram positive and Gram negative pathogens such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae.* The most gruelling part is that these pathogens are multidrug resistant (Saad Nseir *et al.,* 2008). VAT is associated with increased duration of mechanical ventilation, ICU stay and hospital costs (Nseir *et al.,* 2005). Appropriate antibiotic therapy after serial culture and sensitivity of the tracheal secretions is needed to reduce the risk of progression of VAT to VAP (Craven *et al.,* 2016).

Many studies have focused on the study of VAP. But there are very few articles regarding VAT. The current article emphasizes the incidence, microbiology, multidrug resistance in the pathogens which can be a guide to the treating physician.

Materials and Methods

This was a prospective study which was done for a period of one year in the ICU complex of a tertiary care hospital after obtaining Institutional ethical clearance.

Inclusion criteria

Patients who were admitted and underwent mechanical ventilation > 24 hours in the age group > 18 years

Exclusion criteria

Patients with respiratory problems on admission like COPD (Chronic obstructive pulmonary disease), tuberculosis, Asthma and ARDS (Acute respiratory distress syndrome).

Materials and Methods

The study was conducted in the ICU complex of a tertiary care hospital. A total of 149 patients on ventilator were included. The cases included both males and females more than 18 years who were on mechanical ventilation. All patients having respiratory system disorders like COPD, Asthma, Tuberculosis were excluded from the study.

A proforma was prepared and the relevant details like age, sex, diagnosis at the time of admission, indication and date of ventilation, ventilation mode and settings, antibiotics given, investigations done, chest X-ray findings, duration of ventilation, ICU stay and hospital stay were noted. The patient was monitored from the date of admission till the date of discharge and the outcome was noted.

The endotracheal aspirates were collected using a mucous extractor. The samples were transported to the laboratory with minimal delay and were processed immediately to prevent the overgrowth of bacterial pathogens.

A Gram stain was performed and the sample cultured on 5% Sheep Blood agar, Chocolate agar and incubated at 35ºC for 24 hours and on Sabouraud's dextrose agar at 24 ºC for 48 hours. The routine biochemical tests were performed and antimicrobial susceptibility testing done by Kirby Bauer method as per CLSI (Clinical and laboratory standards institute) guidelines.

Antimicrobial susceptibility testing

The purpose of the Kirby-Bauer disk diffusion susceptibility test was done to determine the sensitivity or resistance of pathogenic bacteria to various antimicrobial drugs.

Inoculation of the Mueller Hinton agar plate

A lawn culture of the test bacteria was applied on the Mueller Hinton agar plate. The appropriate antimicrobial impregnated disks were placed on the surface of the agar using forceps and the lid was replaced and incubated at 35°C for 16-18 hours.

Following incubation, the zone sizes were measured. Using the published CLSI guidelines, the susceptibility or resistance of the organism to each drug tested was noted.

The results of the Kirby-Bauer disk diffusion susceptibility test were reported only as susceptible, intermediate, or resistant.

Antibiotics tested

Gram positive bacteria

Penicillin (10U), Cefoxitin (30µg), Gentamicin (10 µg), Erythromycin (15 µg), Clindamycin (2 µg), Cotrimoxazole (1.25/23.75 µg), Ciprofloxacin (5µg), Linezolid (30 µg), Teicoplanin (30µg), Vancomycin (30µg)

In the case of *Enterococcus*, Ampicillin (10 µg), High level Gentamicin (120 µg), Ciprofloxacin (5µg), Linezolid (30 µg), Teicoplanin (30µg), Vancomycin (30µg) were used.

Enterobacteriaceae

Ampicillin (10 µg), Ceftazidime (30µg), Ceftriaxone (30µg), Cefotaxime (30µg), Cefepime (30µg), Cefoperazone Sulbactam (75/30µg), Piperacillin Tazobactam (100/10 µg), Amikacin (30 µg), Ciprofloxacin (5 µg), Cotrimoxazole (1.25/23.75 µg),Imipenem (10 µg), Meropenem (10 µg), Tigecycline (15µg), Colistin (10µg).

Pseudomonas

Ceftazidime (30 µg), Ceftriaxone (30 µg), Cefepime (30µg), Cefoperazone Sulbactam (75/30µg), Piperacillin Tazobactam (100/10 µg), Amikacin (30 µg), Ciprofloxacin (5µg), Cotrimoxazole (1.25/23.75 µg), Imipenem (10 µg), Meropenem (10 µg), Doripenem (10 µg), Tigecycline (15µg), Colistin (10µg).

Acinetobacter

Ceftazidime (30µg), Ceftriaxone (30µg), Cefotaxime (30µg), Cefepime (30µg), Cefoperazone Sulbactam (75/30µg), Piperacillin Tazobactam (100/10 µg), Amikacin (30µg), Ciprofloxacin (5µg), Cotrimoxazole (1.25/23.75 µg), Imipenem (10 µg), Meropenem (10 µg), Tigecycline (15µg), Colistin (10µg).

Results and Discussion

The total number of patients in our study was 149 among which 37 (24.83%) developed VAT and 30 (20.13%) were colonisers of the respiratory tract.

Out of the149 patients, 101 (67.78%) were males and 48 (32.22%) were females. Males predominated the study (Fig. 1).

The maximum numbers of cases were seen in the age group of 41 to 60 years (43.62%) followed by 61-80 years (37.58%) (Fig. 2).

The most common reason for RICU admission in our hospital was Multisystem involvement (40.27%), Central nervous system disorders (25.51%) followed by Kidney diseases (14.09%), Coronary artery disease (4.7%) (Fig. 3).

Liver diseases (2.68%) and miscellaneous causes which includes Road traffic accident, Snake bite, Poisoning and Undiagnosed fever (12.75%).

Among the 37 patients who developed VAT, 28 (75.68 %) were males and 9 (24.32 %) were females (Fig. 4).

82.76 % were ventilated for poor GCS (Glascow coma scale), 12. 07% for desaturation and 5.17 % for airway protection (Fig. 5).

Among the 37 VAT patients, 51.35 % were smokers, 40.54 % were alcoholics, 5.41 % were addicted to both alcohol and smoking and 2.7 % did not smoke or consume alcohol (Fig. 6).

The maximum prevalence was seen in the age group of 41 -60 years (40.54%) followed by 61-80 years (32.43%)

43.24 % of VAT patients had multisystem disorders, 24.32% has kidney disorders, 18.92% had central nervous system disorders, 5.41% had cardiovascular system involvement and 8.11% were admitted with poisoning, road traffic accidents and carcinomas (Fig. 7).

32.76% had hypertension, 25.86% had diabetes, 17.24% had both diabetes and hypertension and 24.14% had no co morbidities (Fig. 8).

89.66% had one organism in endotracheal aspirate and 10.34% had two organisms (Fig. 9).

Acinetobacter baumannii was responsible for 33.33 % of VAT infections followed by *Klebsiella pneumoniae* (22.22%), *Pseudomonas aeruginosa* (8.89%), *Staphylococcus aureus* (11.11%), *Candida albicans* (13.33%), *Escherichia coli* (4.44%), *Citrobacter*, *Enterococcus*, *Proteus* each 2.22%.

Ventilator associated tracheobronchitis is an important ventilator associated respiratory infection in the ICU. Its prevalence varies from 1.4 % to 9 % (Nseir and Martin-Loeches, 2014). It is an important cause of increased morbidity and mortality in hospitals. The present study was undertaken in the RICU complex of a tertiary care hospital. After excluding patients with respiratory system disorders on admission and patients who developed VAP, a total of 149 patients were allotted for the study out of which 67.78 % were males and 32.22 % were females. The maximum numbers of cases were seen in the age group of 41 to 60 years (43.62%) followed by 61-80 years (37.58%).

The most common reason for RICU admission in our hospital was Multisystem involvement (40.27%), Central nervous system disorders (25.51%) followed by Kidney diseases (14.09%), Coronary artery disease (4.7%), Liver diseases (2.68%) and miscellaneous causes which includes Road traffic accident, Snake bite, Poisoning and Undiagnosed fever (12.75%).

The incidence of VAT in our study was 24.83%. The incidence of VAT reported in other studies were 15 % by *Lei et al.,* and 13.2 % by *Ray et al.,* which is lower compared to our study. The increased prevalence in our study may be due to the increased number of patients who were admitted with multisystem disorders and infection with virulent and multi drug resistant pathogens,

Among the 37 patients who developed VAT, 28 (75.68 %) were males and 9 (24.32 %) were females. This is in contrast to the study by *Dallas et al.,* in which 50% were males and 50% were females but similar to *Ray et al.,* who reported 75% of males and 25% of females (Dallas *et al.,* 2011).

82.76 % of patients were ventilated for poor GCS, 12.07 % for desaturation and 5.17 % for airway protection. 32.76% had hypertension, 25.86% had diabetes, 17.24% had both diabetes and hypertension and 24.14% had no

co morbidities. *Mayuri et al.,* reported 37.2% of patients with diabetes and 30% of patients with hypertension (Mayuri, 2017). *Sadek et al.,* reported 20% of diabetics and 40% of hypertension patients in VAT patients (Sadek *et al.,* 2014).

Among the 37 VAT patients, 51.35 % were smokers, 40.54 % were alcoholics, 5.41 % were addicted to both alcohol and smoking and 2.7 % did not smoke or consume alcohol.

The increased incidence (40.54 %) was seen in the age group of 41-60 years followed by 61-80 years (32.43 %)

Hashemi et al., in their study identified 33% in the 70-89 years, 26% in the 50-69 years age group followed by 24.6% in 30-49 years which is different from our study (Hashemi *et al.,* 2017).

But *Mayuri et al.,* in their study reported 18% of patients in the age group of 41-50 years and 13% in the 50 -60 years age group which is similar to our study (Mayuri, 2017).

43.24 % of VAT patients had multisystem disorders, 24.32% has kidney disorders, 18.92% had central nervous system disorders, 5.41% had cardiovascular system involvement and 8.11% were admitted with poisoning, road traffic accidents and carcinomas. *Nseir et al.,* in their study reported 21% of patients with central nervous system disorders and 25% of patients with kidney disorders and 20% of patients with cardiac problems (Nseir *et al.,* 2005).

89.66 % of isolates were monomicrobial and 10.34 % of isolates were polymicrobial yielding a total of 68 isolates. This is in controversy to the study by *Sadek et al.,* who reported 40% of polymicrobial VAT and the causative organisms were *Acinetobacter* and *Pseudomonas* (40%) (Sadek *et al.,* 2014). Gram negative pathogens were responsible for 75.54% of VAT infections followed by 13.33% of Gram positive bacteria. *Karvouniaris et al.,* reported 92.9% of VAT caused by Gram negative bacteria (Karvouniaris *et al.,* 2013). *Acinetobacter baumannii* was responsible for 33.33 % of VAT infections followed by *Klebsiella pneumoniae* (22.22%), *Staphylococcus aureus (11.11%), Pseudomonas aeruginosa* (8.89%), *Escherichia coli* (4.44 %), *Citrobacter, Enterococcus, Proteus* each 2.22%. *Candida albicans* was responsible for 13.33% of VAT infections.

The most common pathogen of VAT was *Pseudomonas aeruginosa* 52.3% followed by *Klebsiella pneumoniae* 20.8% in a similar study by (*Babu et al.,* 2011).

In a study by *Mayuri et al., Pseudomonas aeruginosa* was the predominant pathogen isolated (29%) followed by *Klebsiella pneumoniae* (26%), *Acinetobacter baumannii* (20%), *Staphylococcus aureus* (12%), *Escherichia coli* (8%) and *Citrobacter freundii* (6%) (Mayuri, 2017).

In a study by *Dallas et al.,* Gram negative bacteria (50%) were the predominant causative organisms of VAT when compared to Gram positive bacteria (37.5%).

MRSA was the predominant bacteria (18.8%) followed by *Acinetobacter baumannii* (15.6%), *Pseudomonas aeruginosa* (9.4%) (Dallas *et al.,* 2011).

Acinetobacter baumannii was responsible for 33.33 % of cases with VAT.

It is a virulent bacteria and very resistant to adverse conditions and is an emerging pathogen of nosocomial infections, particularly patients admitted in the ICU and on mechanical ventilation (Manchanda *et al.,* 2010) (Table 1–5).

Fig.1 Gender distribution of the study group

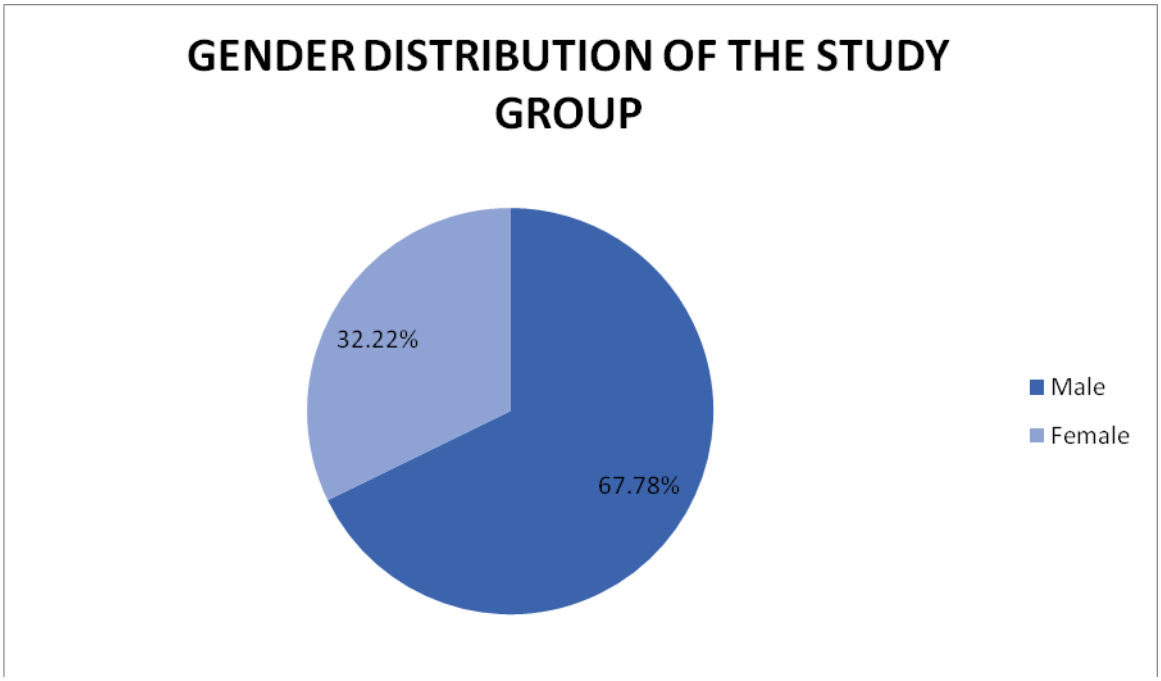

Fig.2 Age distribution of the study group

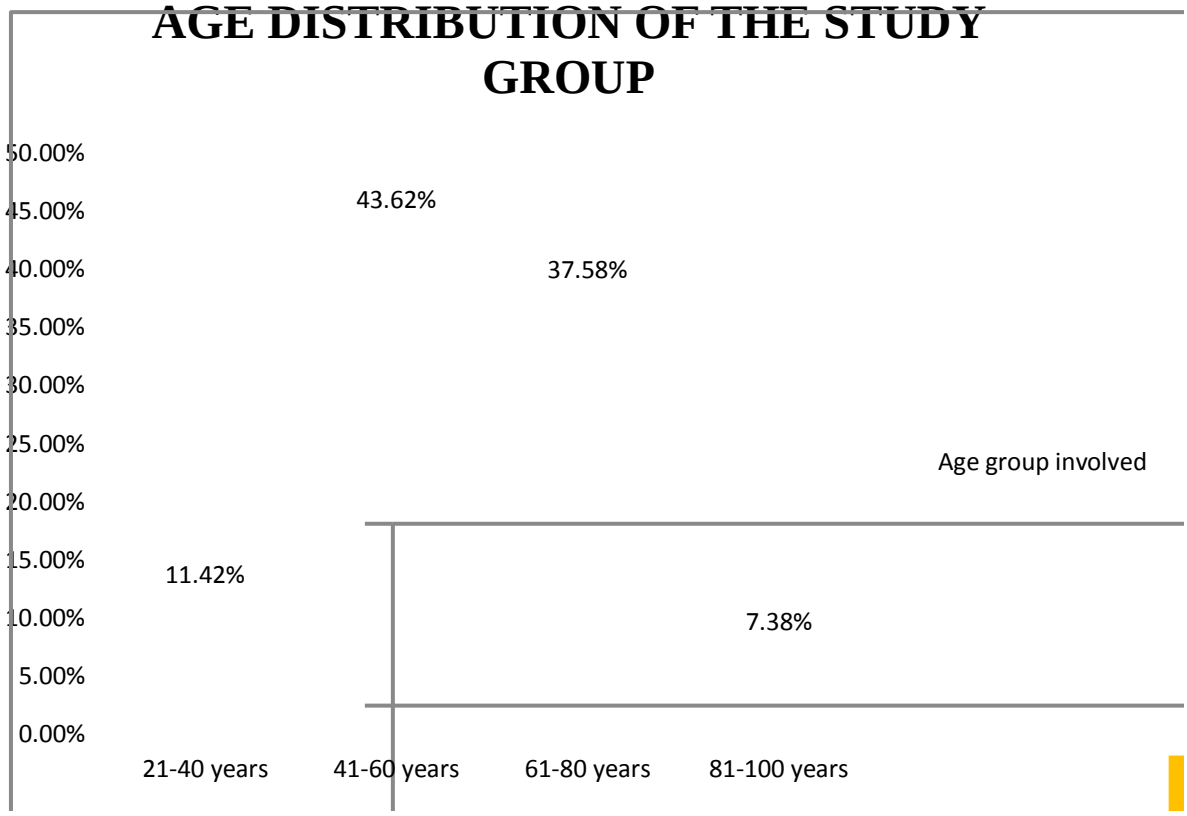

Fig.3 Distribution of study group by diagnosis

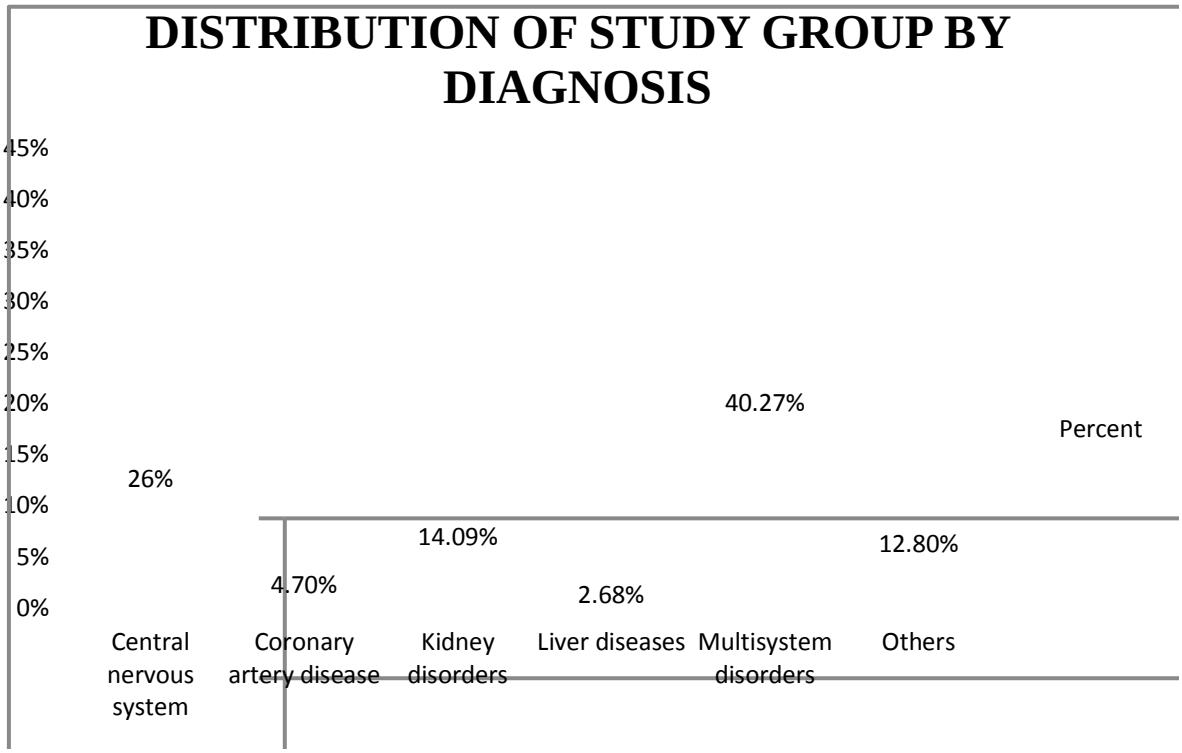

Fig.4 Gender distribution of VAT patients

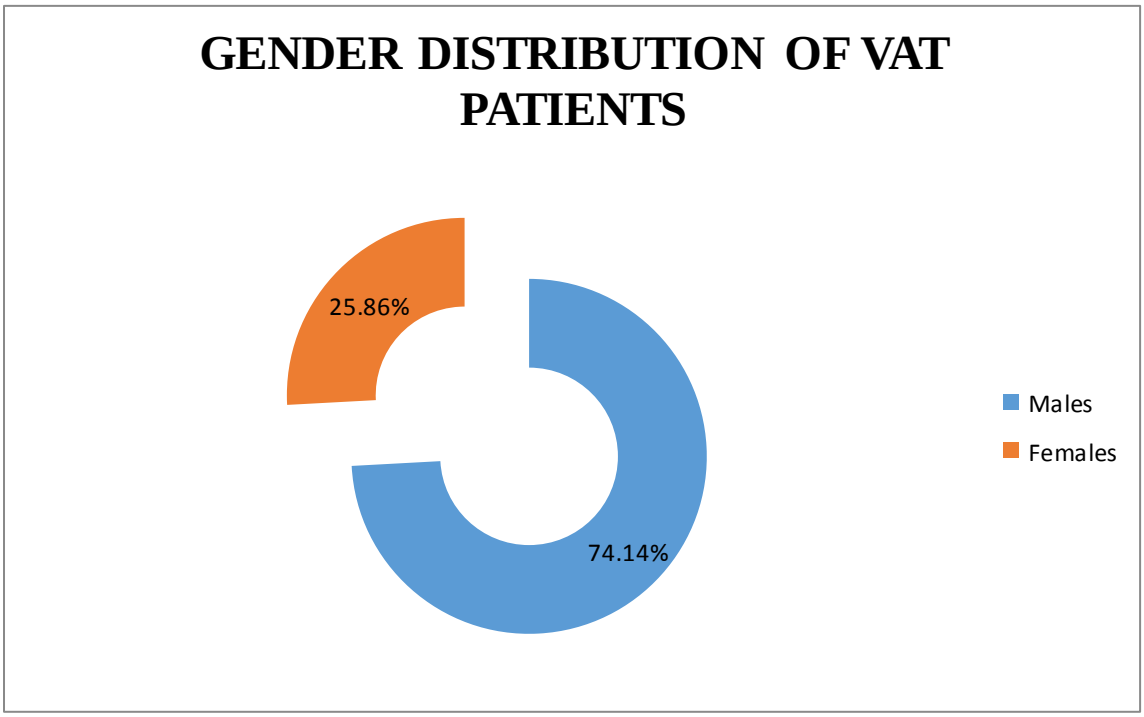

Fig.5 Indications for ventilation in VAT patients

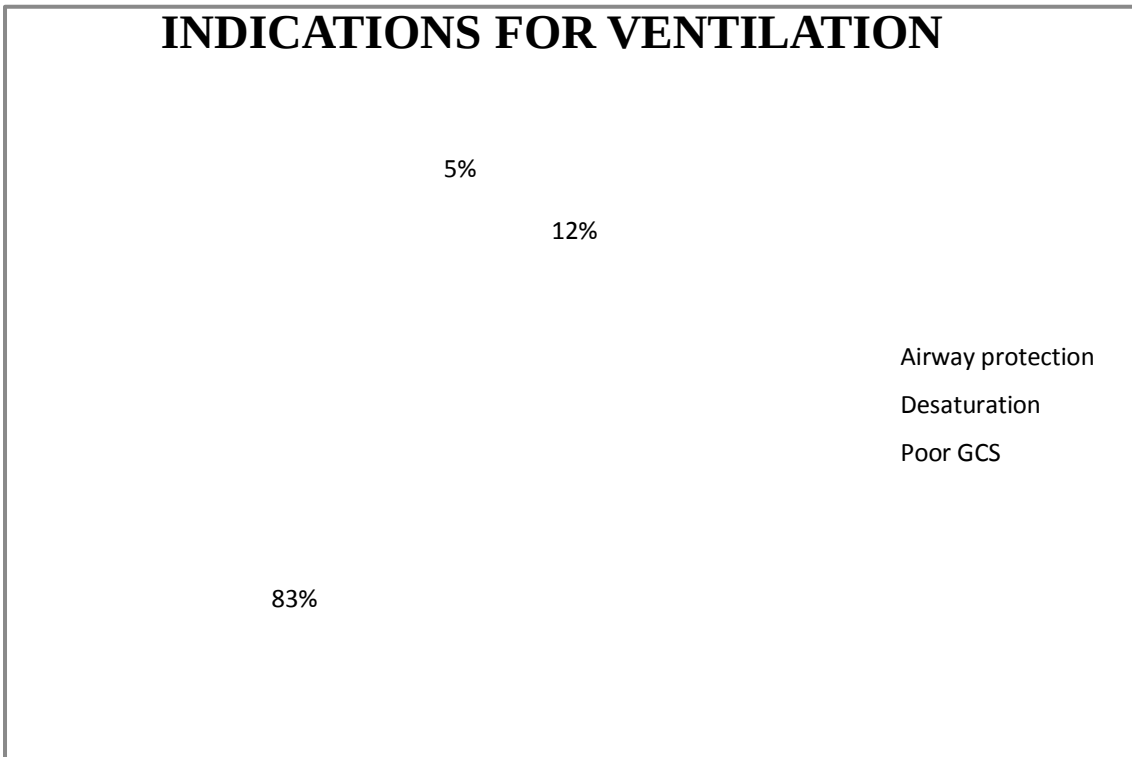

Fig.6 Distribution of VAT patients by personal habits

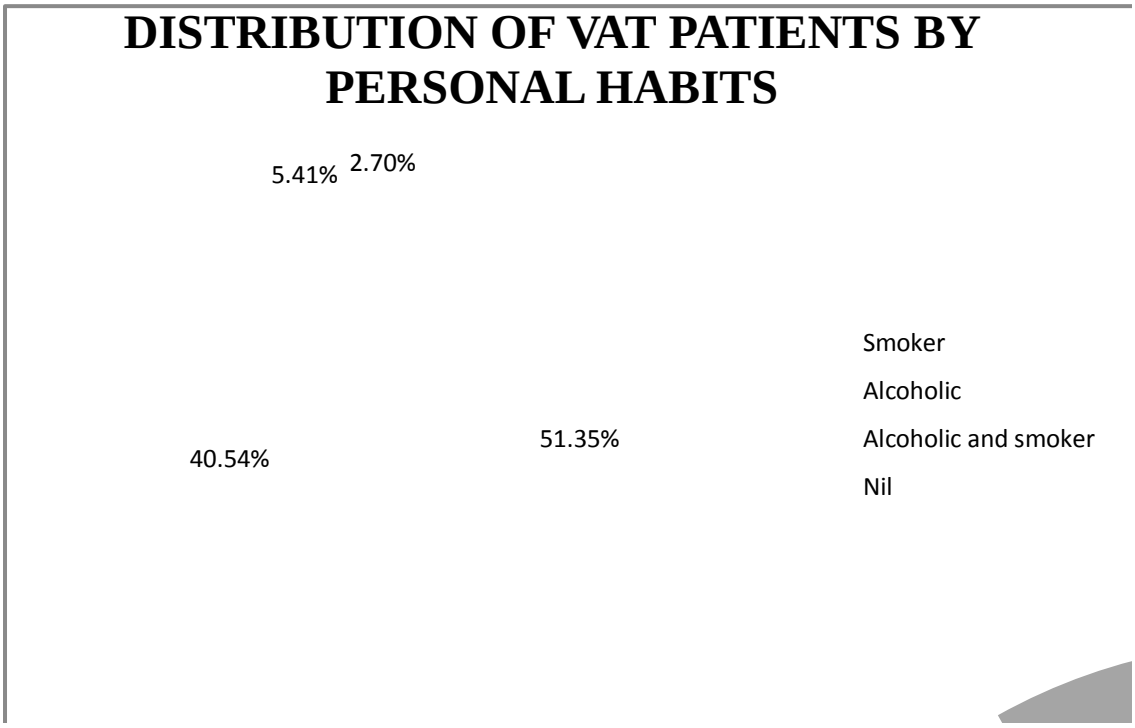

Fig.7 Distribution of VAT patients by diagnosis

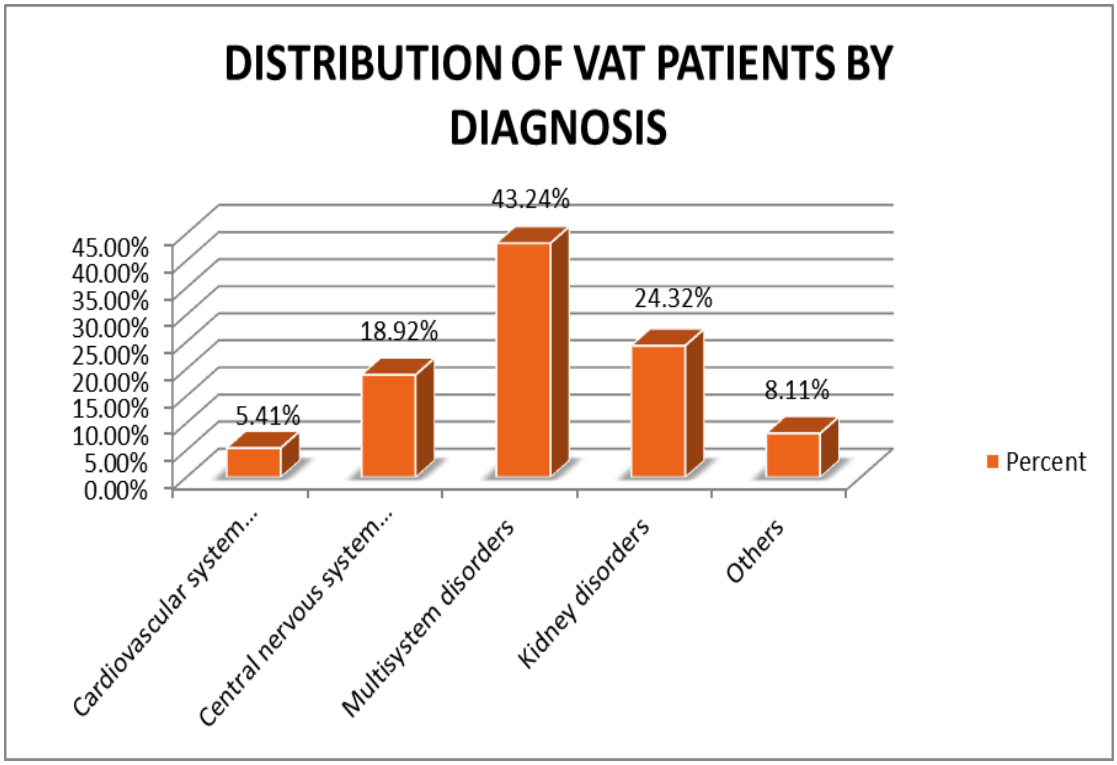

Fig.8 Distribution of VAT patients by co morbidities

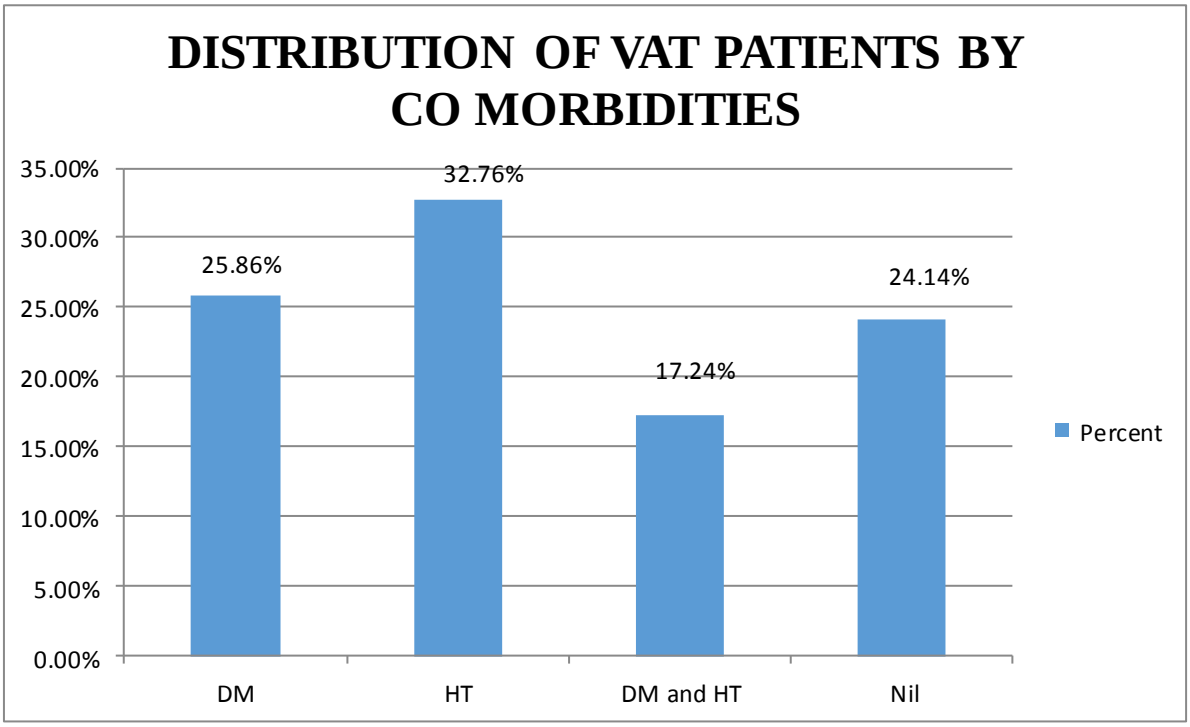

Fig.9 Monomicrobial and polymicrobial VAT

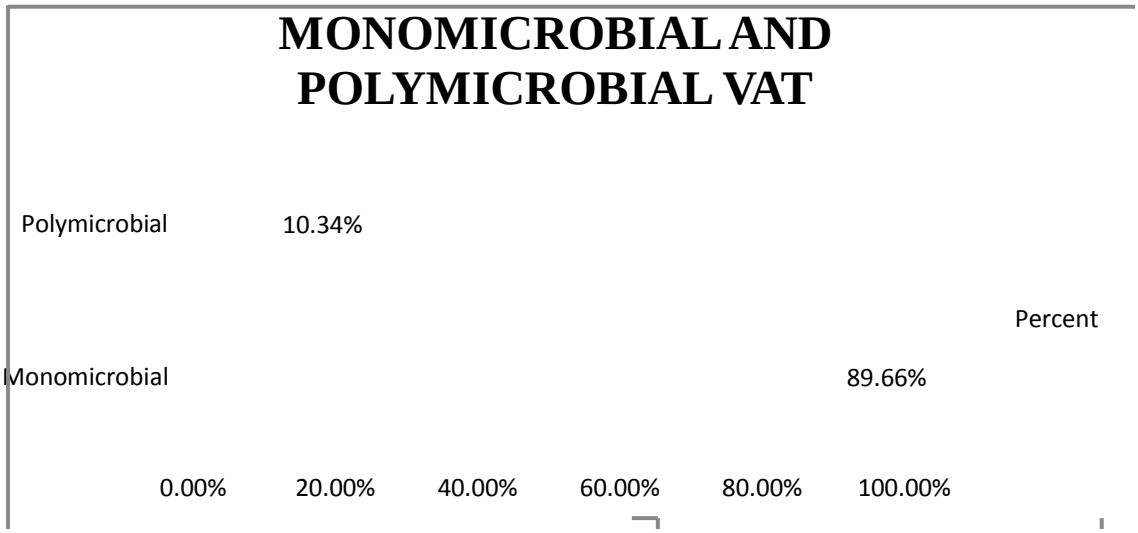

Fig.10 Antibiotic resistance pattern in *Acinetobacter* and *Pseudomonas*

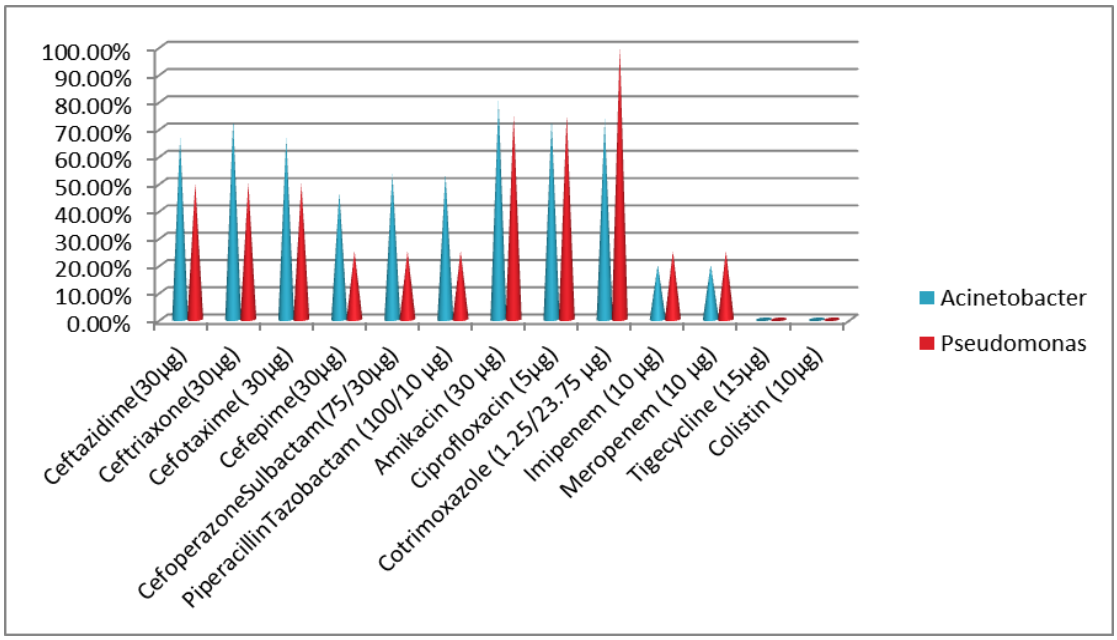

Table.1 Distribution of VAT patients by age group

AGE GROUP	MALE	FEMALE	TOTAL
21-40	5	1	6 (16.22%)
41-60	11	4	15(40.54%)
61-80	9	3	12(32.43%)
81-100	3	1	4(10.81%)

Table.2 Microbiological profile of VAT

S.NO	ORGANISM	NUMBER	PERCENT
1.	*Acinetobacter baumannii*	15	33.33%
2.	*Klebsiella pneumoniae*	10	22.22%
3.	*Pseudomonas aeruginosa*	4	8.89%
4.	*Staphylococcus aureus*	5	11.11 %
5.	*Escherichia coli*	2	4.44 %
6.	*Candida albicans*	6	13.33 %
7.	*Enterococcus*	1	2.22%
8.	*Citrobacter*	1	2.22%
9.	*Proteus*	1	2.22%

Table.3 Antibiotic resistance in gram positive bacteria

Antibiotic disks	*Staphylococcus aureus* (n=5)		*Enterococcus* (n=1)	
	S	R	S	R
Penicillin(10U)	0	100%	NT	NT
Ampicillin (10µg)	NT	NT	0	100%
Cefoxitin(30µg)	40%	60 %	NT	NT
Gentamicin(10µg)	40 %	60 %	NT	NT
High level Gentamicin	NT	NT	100%	0
Erythromycin(15µg)	40 %	60 %	0	100%
Clindamycin(2µg)	60 %	40 %	NT	NT
Cotrimoxazole(1.25 /23.75µg)	40 %	60 %	NT	NT
Ciprofloxacin(5 µg)	40%	60 %	0	100%
Linezolid(30µg)	100%	0	100%	0
Teicoplanin(30µg)	100%	0	100%	0
Vancomycin(30µg)	100%	0	100%	0

Table.4 Antibiotic resistance in gram negative bacteria

Antibiotic disks	*Escherichia coli* (n=2)		*Klebsiella pneumoniae* (n=10)		*Citrobacter* (n=1)		*Proteus* (n=1)	
	S	R	S	R	S	R	S	R
Ampicillin (10µg)	0	100%	NT	NT	0	100%	0	100%
Ceftazidime (30µg)	50%	50%	60%	40%	0	100%	0	100%
Ceftriaxone (30µg)	50%	50%	60%	40%	0	100%	0	100%
Cefotaxime (30µg)	50%	50%	60%	40%	0	100%	0	100%
Cefepime (30µg)	100%	0	80%	20%	100%	0	100%	0
Cefoperazone Sulbactum (75/30µg)	100%	0	80%	20%	0	100%	0	100%
Amikacin (30 µg)	0	100%	30%	70%	0	100%	0	100%
Ciprofloxacin (5 µg)	0	100%	50%	50%	0	100%	0	100%
Cotrimoxazole (1.25/23.75 µg)	0	100%	40%	60%	0	100%	0	100%
Imipenem (10 µg)	50%	50%	80%	20%	100%	0	100%	0
Meropenem (10 µg)	50%	50%	80%	20%	100%	0	100%	0
Tigecycline (15µg)	100%	0	100%	0	100%	0	100%	0
Colistin (10µg)	100%	0	100%	0	100%	0	NT	NT

Table.5 Comparison of incidence and gender distribution with other studies

S. No	Author	Incidence (%)	Males	Females	Reference
1.	Lei *et al.*,	15%	73.5%	26.5%	(8)
2.	Ray *et al.*,	13.2%	75%	25%	(9)
3.	Dallas *et al.*,	1.4%	50%	50%	(10)
4.	Mayuri *et al.*,	16.7%	69%	31%	(11)
5.	Present study	24.83%	75.68%	24.32%	

Multidrug resistance (MDR) is defined as resistance to more than two groups of antibiotics (Magiorakos *et al.*, 2012). 53.33 % of *Acinetobacter* strains, 40 % of *Klebsiella pneumoniae*, 75 % of *Pseudomonas aeruginosa*, 100 % of *Escherichia coli*, 100 % of *Citrobacter*, 60 % of *Staphylococcus aureus* were found to be multidrug resistant.

66.67% of *Acinetobacter* isolates were resistant to Ceftazidime and Cefotaxime, 46.67 % to Cefepime, 53.33% to Piperacillin Tazobactum and Cefoperazone Sulbactum, 80% to Aminkacin. Only 20% of the isolates were resistant to Carbapenems proving their effectivesness in VAT infections. All isolates were sensitive to Tigecycline and Colistin (Fig. 9).

60% of *Klebsiella pneumoniae* isolates were resistant to Ceftazidime, Cefotaxime and Ceftriazone. 20% to Cefoperazone Sulbactum and Cefepime, Imipenem and Meropenem, 50% to Ciprofloxacin and 70% to Amikacin.

Among *Pseudomonas aeruginosa*, 50% of isolates were resistant to Ceftazidime, Ceftriazone and Cefotaxime, 25 % to Cefaperazone Sulbactum, 75% to Amikacin and Ciprofloxacin, 25% to Imipenem and Meropenem.

Among *Escherichia coli* isolates, 50% were resistant to Cefotaxime and Ceftriaxone, 100 % to Amikacin and Ciprofloxacin, 50% to Imipenem and Meropenem. None of the isolates were resistant to Tigecycline and Colistin.

Among *Staphylococcus aureus* isolates, 60% were MRSA, 60% resistant to Ciprofloxcin, Cotrimoxazole, Erythromycin and Gentamicin. All the isolates were sensitive to Linezolid and Vancomycin.

The increased prevalence of MDR infections were due to the increased use of fourth generation Cephalosporins in the ICU on admission.

Babu et al., in their study reported 24% of resistance in Amikacin, 96% in Cefotaxime, 31% in Cefoperazone Sulbactum, 36% in Cefpirome and 22 % in Ciprofloxacin. Among Klebsiella isolates, 22% in Amikacin, 61% in Cefoperazone Sulbactum, 43% in Ceftazidime, 20% in Ciprofloxacin. Among *Pseudomonas aeruginosa* isolates, 55% in Cefoperazone Sulbactum, 87% in Ceftazidime, 25 % in Ciprofloxacin (Babu *et al.*, 2011).

In a study by *Ray et al.,* 100 % of *Acinetobacter baumannii* and 33 % of *Pseudomonas aeruginosa were MDR.*

Nseir et al., in their study reported 54% VAT episodes were polymicrobial and 56% were related to multidrug-resistant bacteria (Nseir *et al.*, 2005).

78.7% isolates were multi drug resistant in a study by Mayuri (2017).

20.35% of VAT cases were due to pan drug resistant isolates. Imipenem resistance of, 21.43%, 33.3% and 44.82% among *Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Acinetobacter baumanii* respectively was observed in a similar study (Babu *et al.*, 2011).

Isolates were found to be pan resistant was reported by *Álvarez Lerma et al.,* Fortunately there was no panresistant isolates in our study (Francisco Álvarez Lerma *et al.*, 2017). In such cases Ceftalozane Tazobactum, a newly discovered Cephalosporin was found to be useful.

The mean days spent on mechanical ventilation was found to be 6.51± 2.88 days.

The mean number of days spent in the ICU was found to be 8.76 ± 7.68 days. The mean hospital days were 14.78 ± 9.92 days.

The duration of mechanical ventilation for VAT patients was 21.6 ± 16.0 days and the length of ICU stay was 28.0 ± 15.7 days in a similar study (Nseir *et al.,* 2005). In another study by *Dallas et al.,* the duration of mechanical ventilation was 16.5 ± 13.3 days, ICU days 17.3 ± 11.0 and hospital days 26.6 ± 16.7 days which is higher compared to our study (Dallas *et al.,* 2011).

Babu et al., reported 12 ± 2.1 days hospital stay in VAT patients (Babu *et al.,* 2011).

18.92 % of patients outcome ended in death and 37.84 % of patients improved. The outcome of other VAT patients could not be assessed in our study because most of the patients got discharged at request at a critical condition. *Nseir et al.,* observed a mortality of 55% and *Dallas et al.,* 20% (Nseir *et al.,* 2002; Dallas *et al.,* 2011).

VAT caused by MDR pathogens continues to be a threat to the hospital environment. It is associated with increased mortality, increased duration of mechanical ventilation, ICU stay in the hospital (Keyt *et al.,* 2014).

A proper ventilator care bundle should be implemented. Proper weaning measures, sedation holidays should be done to reduce the duration of patients on mechanical ventilation (Shahabi *et al.,* 2016).

A strict antibiotic policy should be framed and adhered to strictly to cut down the rate of multi drug resistance. Inhaled antibiotics can be given to reduce the risk of ventilator associated respiratory infections (Palmer *et al.,* 2008). More research should be done in the future to know the local resistance patterns of the isolates causing ventilator associated respiratory infections.

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How to cite this article:

Nanthini Devi, P. and Gomathi, S. 2018. A Study of Incidence and Microbiological Profile of Ventilator Associated Tracheobronchitis (VAT) in a Tertiary Care Hospital. *Int.J.Curr.Microbiol.App.Sci.* 7(04): 907-921. doi: https://doi.org/10.20546/ijcmas.2018.704.097