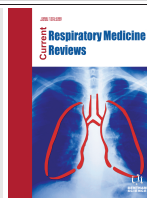


RESEARCH ARTICLE


**BENTHAM
SCIENCE**

Bacterial Profile and Antibiotic Use in Pneumonia Patients at Dr. Soetomo General Hospital



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Abstract: Background: Pneumonia is one of the causes of morbidity and mortality in children and adults worldwide. WHO report in 1999 stated that the main cause of death due to infectious disease is pneumonia. The rising mortality rate among severe pneumonia patients is because they do not receive empirical antibiotic treatment according to the infecting pathogens.

Objective: The purpose of this study is to identify the bacterial profile and the use of antibiotic treatment on pneumonia patients admitted to the pulmonology ward of Dr. Soetomo General Hospital in Surabaya, Indonesia.

Methods: This descriptive observational study used the data from pneumonia patients admitted to the pulmonology ward of Dr. Soetomo General Hospital, Surabaya, from February to April 2018. The data was collected from the patients' medical records, antibiotic use notes, and culture results of bacterial antibiotic sensitivity test. The total of antibiotic use was calculated using a defined daily dose (DDD) per 100 bed days. The quality of antibiotics was assessed using Gyssens method. The microbial mapping was acquired from a sputum culture test result.

Results: The most prevalent bacteria in pneumonia patients were the Gram-negative bacteria and the most common species was *Acinetobacter baumannii* followed by *Klebsiella pneumoniae*. In contrast, the most common Gram-positive bacteria species was *Streptococcus viridans*. The total antibiotic use was 35.53 DDD/100 bed days, and ceftriaxone was the most commonly used antibiotic with 9.23 DDD/100 bed days. Fifty percent of the antibiotic use was in category wise use of antibiotic.

Conclusion: The Gram-negative bacteria were the most common cause of pneumonia and ceftriaxone was the most commonly used antibiotic for its cure. Fifty percent of the patients received ceftriaxone appropriately.

Keywords: Antibiotic, bacterial profile, defined daily dose, Gyssens method, infection, pneumonia.

1. INTRODUCTION

Pneumonia is one of the infectious diseases that still is prevalent in society, especially in developing countries. Pneumonia is one of the most common causes of morbidity and mortality among children and adults worldwide [1]. SEAMIC Health Statistics data in 2001 states that pneumonia is the third cause of death in Singapore and Vietnam and

places sixth in Indonesia and Thailand, seventh in Malaysia and ninth in Brunei [2]. In East Java, Indonesia, the prevalence of pneumonia in 2016 was 26.76% of the population [3]. Pneumonia patients in the pulmonology ward of Dr. Soetomo General Hospital were treated with antibiotic, to improve their condition and prevent the incidence of microbial resistance. However, the mortality rate is still sky-high, reaching 33% to 50%.

Pneumonia patients are provided with antibiotic(s) and supportive treatment. Antibiotic treatment is given through microorganism data and sensitivity test result. However, the culture process requires time, therefore, empirical antibiotic

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therapy is given to close the gap. The choice of empirical antibiotic is adjusted to the microbial sensitivity pattern in the ward. Empirical antibiotic is chosen from a wide spectrum group, to combat a wide range of pathogen possibilities. The uncontrolled usage of wide spectrum antibiotic treatment may cause unwanted outcomes such as the adverse effects of the drug or the likeliness of microbial resistance. Moreover, it may cause multiple problems, such as the incidence of superinfection, the soaring cost of medical treatment, more toxic adverse effects, and patients' duration of stay [4].

In a multiple center study of antibiotic usage, 30% to 80% of antibiotic usage is not in line with the indication [5]. In a study of pneumonia patients in Dr. Kariadi General Hospital in Semarang, Indonesia, microbial resistance occurred in several community-acquired pneumonia (CAP). The resistance occurred in 55% of *Streptococcus pneumoniae* towards oxacillin, and 100% in *Staphylococcus haemolyticus* towards cefotaxime. While in nosocomial pneumonia, bacterial resistance occurs in 100% of *Acinetobacter baumannii* towards amoxicillin with clavulanic acid [6].

The usage of antibiotic in pneumonia treatment is not only a formality to complete the treatment but the usage needs to be controlled with highly intensive monitoring for excessive antibiotic usage which will increase the incidence of resistance. This phenomenon become a national and global focus. World Health Organization (WHO) has established Defined Daily Dosage (DDD) that then can compare the DDD per 100 bed days between time frame, another ward, another hospital, etc. and DU 90% as standardized methods in drug use study, and the advantage of the comparison in this study is to briefly illustrate the data [7]. WHO recognizes this method as an internationally applied standard in drug use study.

All hospitals in Indonesia, including Dr. Soetomo General Hospital, are currently preparing antibiotic stewardship strategy through the formation of antibiotic resistance controlling program (ARCP) team, according to ministerial order of the Ministry of Health, no 8, 2015 [8]. The purpose of this study is to identify the antibiotic usage profile qualitatively and quantitatively based on the microbial characteristic of pneumonia patients in the pulmonology ward in Dr. Soetomo General Hospital. Moreover, the data is expected to be used as supplementing data in perfecting the antibiotic usage guidelines and supporting the development of ARCP in Dr. Soetomo General Hospital, Surabaya, Indonesia.

2. MATERIAL AND METHODS

This study was a descriptive observational study conducted at Dr. Soetomo General Hospital in Surabaya, Indonesia from February 2018 to April 2018. This study used the data of pneumonia patients admitted in pulmonology ward of Dr. Soetomo General Hospital in Surabaya. The data were taken using a purposive sampling technique based on the inclusion and exclusion criteria. The inclusion criteria of this study were patients age 18 years old and above, receiving antibiotic prescription but have not

used the antibiotic before the culture. The exclusion criteria of this study were patients with other infections than pneumonia. The data used in this study were drawn from patients' medical records, including the notes of antibiotic use, and culture results of bacterial antibiotic sensitivity test. The total use of antibiotic was calculated using DDD per 100 bed days. The quality of antibiotic was assessed using Gyssens method [9]. The microbial pattern was acquired from sputum culture test result.

2.1. Statistical Analysis

Antibiotic usage profile was analyzed by summarizing the count of antibiotic use based on DDD per 100 bed days and Gyssens method. The data were analyzed using SPSS 17.0.0 for Windows software, 2007, SPSS Inc. Chicago, IL, USA, and Microsoft Office 2013.

2.2. Ethical Clearance

This study followed the principles of the Declaration of Helsinki. This study had received ethical clearance from Dr. Soetomo General Hospital before the study begins (Ethical Clearance Number 0061/KEPL/II/2018). Details that might disclose the identity of the subjects under study were omitted.

3. RESULTS

3.1. Sample Characteristics

A total of 153 pneumonia patients were admitted to the pulmonology ward of Dr. Soetomo General Hospital from February 2018 to April 2018. Based on the inclusion and exclusion criteria, 74 patients - comprising of 43 males (58.11%) and 31 females (41.89%) - were included in this study. Pneumonia mostly affected those older than 55 years old and the length of the stay (LoS) of the pneumonia patients was mostly between 7 and 14 days (Table 1).

Table 1. Characteristics of subjects in the study.

-	N	%
Gender		
Male	43	58.11
Female	31	41.89
Age		
18-25 years old	1	1.35
26-55 years old	33	44.59
>55 years old	40	54.06
Length of Stay		
<7 days	16	21.62
7-14 days	39	52.7
15-21 days	12	16.22
>21 days	7	9.46

Table 2. Bacterial profile from sputum culture.

Types of Bacteria	-	N	%
Gram-positive	<i>Streptococcus viridans</i>	18	22.50
	<i>Staphylococcus coagulase negative</i>	7	8.75
	<i>Staphylococcus aureus</i>	3	3.75
	<i>Gemella morbillorum</i>	2	2.50
	<i>Streptococcus sanguinis</i>	1	1.25
Gram-negative	<i>Acinetobacter baumannii</i>	12	15
	<i>Klebsiella pneumoniae</i>	12	15
	<i>Acinetobacter spp</i>	3	3.75
	<i>Enterobacter cloacae</i>	3	3.75
	<i>Pseudomonas aeruginosa</i>	3	3.75
	<i>Escherichia coli</i>	2	2.5
	<i>Enterobacter aerogenes</i>	2	2.5
	<i>Achromobacter species</i>	1	1.25
	<i>Aeromonas caviae</i>	1	1.25
	<i>Burkholderia cepacia complex</i>	1	1.25
	<i>Pseudomonas putida</i>	1	1.25

3.2. Bacterial Profile

Based on the culture results of 74 patients, 17 species of bacteria were found, consisting of five Gram-positive and twelve Gram-negative bacteria. The frequently found Gram-negative bacteria were *Acinetobacter baumannii* and *Klebsiella pneumoniae*. Whereas, the frequently found Gram-positive bacteria were *Streptococcus viridans* (Tables 2 and 6).

3.3. Antibiotic Use

As many as 13 types of antibiotics were given to the patients from February 2018 to April 2018. The total antibiotic use on pneumonia patients admitted to the pulmonology ward in Dr. Soetomo General Hospital from February 2018 to April 2018 was 35.53 DDD/100 bed days (21.09, 54.36, 31.15 respectively). Ceftriaxone was the most commonly used antibiotic with 9.23 DDD/100 bed days (Table 3). Twenty-two patients received combination antibiotic therapy with the most frequently given combination of ceftriaxone and levofloxacin (Table 4). The evaluation of antibiotic use qualitative using the Gyssens method showed that 50% of antibiotic usage was used rationally (Table 5).

4. DISCUSSION

Pneumonia is common in all age groups, but the mortality rate is 2 to 4 times higher in the age group of 60 years old and above than in the age group of 50 years old.

Pneumonia with its high mortality rate is widely known as the forgotten pandemic and transmitted through multiple pathways, such as coughing and sneezing [10]. In addition, no sufficient attention is given by medical professionals.

The results of this study showed that the incidence of pneumonia was higher in males than in females. The finding of this study is in accordance with that from the previous study, where most patients were males [11]. The reason for this is that males are more exposed to greater tendencies of smoking and liquors, which are the CAP risk factors. Smoking habit in healthy adults can increase the risk of lung disease and become the etiology of bronchitis and pneumonia [10]. Other risk factors that can cause pneumonia are low socio-economic status, low nutritional status, low healthcare accessibility, unjust medical practices, and chronic disease sufferer [11].

In this study, pneumonia was found mostly in patients beyond 55 years old. In healthy normal adults, pneumonia is rare due to the defense mechanism of airway and lungs. Risk factors of incidence and mortality caused by pneumonia at later age are higher. Pahriyani (2015) states that the body immunity starts declining when someone reaches 50 years of age [12]. This is due to the change of anatomy and physiology of elderly due to the aging process, which tremendously affects the functional capacity of the lungs, such as the ability to deal with lung function deprivation, the increase in airway resistance towards infections, and the weakening of physical immunity. Farida (2017) reported that

Table 3. DDD/100 bed days calculation of antibiotics used.

Antibiotics	N	%	DDD/100 Bed Days
Ceftriaxone 1 g injection	49	63.64	9.23
Levofloxacin 750 mg intravenous	46	59.74	15.22
Cefixime 100 mg oral	21	27.27	0.88
Ceftazidime 1 g injection	15	19.48	2.56
Meropenem 1g injection	11	14.29	4.34
Levofloxacin 500 mg oral	8	10.39	0.55
Moxifloxacin 400 mg injection	4	5.19	0.55
Cefoperazone Sulbactam 1 g injection	4	5.19	0.52
Azithromycin 500 mg oral	3	3.9	0.31
Gentamicin 80 mg injection	3	3.9	0.81
Cefazolin 1 g injection	2	2.6	0.15
Metronidazole 500 mg intravenous	2	2.6	0.30
Ciprofloxacin 200 intravenous	1	1.3	0.01
Clindamycin 300 mg oral	1	1.3	0.11

Table 4. Antibiotics combination.

Antibiotics Combination	N	%
Ceftriaxone + Levofloxacin	11	50
Meropenem + Levofloxacin	4	18.18
Ceftazidime + Levofloxacin	3	13.64
Ceftazidime + Moxifloxacin	2	9.09
Cefoperazone Sulbactam + Levofloxacin	1	4.55
Meropenem + Moxifloxacin	1	4.55

Table 5. Gyssens method analysis results.

Category	Frequency	%
VI (No sufficient data)	0	0
V (No indication)	0	0
IV A (There is more effective alternative)	0	0
IV B (There is less toxic alternative)	0	0
IV C (There is less costly alternative)	19	25.68

(Table 5) contd...

Category	Frequency	%
IV D (There is less broad spectrum alternative)	0	0
III A (Duration is too long)	5	6.76
III B (Duration is too short)	13	17.57
II A (Incorrect dose)	0	0
II B (Incorrect interval)	0	0
II C (Incorrect route)	0	0
I (Wise use of antibiotic)	37	50

Table 6. Antibiotic sensitivity test pattern.

No.	ATC Code	Antibiotics	<i>Streptococcus viridans</i> (+) N = 18		<i>Acinetobacter baumannii</i> (-) N = 12		<i>Klebsiella pneumoniae</i> (-) N = 12		<i>Acinetobacter spp</i> (-) N = 3		<i>Enterobacter cloacae</i> (-) N = 3		<i>Pseudomonas aeruginosa</i> (-) N = 3		<i>Staphylococcus aureus</i> (+) N = 3	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
-	-	-	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1	J01DB04	Cefazolin	-	-	-	-	3/5	58%	-	-	-	-	1/3	33%	-	-
2	J01DD01	Cefotaxime	-	-	1/2	50%	3/4	75%	1	100%	1	100%	1/3	33%	1/3	33%
3	J01DD02	Ceftazidime	1/18	6%	1/4	25%	5/6	83%	1	100%	1	100%	1	100%	-	-
4	J01DD04	Ceftriaxone	1/18	6%	3/7	42%	1/12	8%	1/3	33%	-	-	-	-	1/3	33%
5	J01DD62	Cefoperazone Sulbactam	1/9	11%	3/4	75%	1/12	8%	1	100%	1	100%	2/3	67%	1/3	33%
6	J01DH02	Meropenem	-	-	3/7	42%	1/12	8%	1	100%	1/3	33%	2/3	67%	-	-
7	J01DH03	Ertapenem	-	-	-	-	1/6	17%	-	-	2/3	67%	-	-	-	-
8	J01DH51	Imipenem	-	-	3/7	42%	1/4	25%	1	100%	1/3	33%	2/3	67%	-	-
9	J01FA01	Erythromycin	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10	J01FF01	Clindamycin	-	-	0	0%	-	-	-	-	-	-	-	-	1/3	33%
11	J01GB01	Tobramycin	1/18	6%	2/3	67%	3/4	75%	-	-	1	100%	2/3	67%	1/3	33%
12	J01GB03	Gentamicin	1/18	6%	2/3	67%	3/4	75%	1	100%	1	100%	2/3	67%	1	100%
13	J01GB06	Amikacin	1/18	6%	3/5	58%	5/6	83%	1	100%	1	100%	1	100%	1/3	33%
14	J01MA02	Ciprofloxacin	1/18	6%	1/2	50%	3/4	75%	1	100%	1	100%	1	100%	1/3	33%
15	J01MA12	Levofloxacin	4/9	44%	2/3	67%	-	-	1	100%	2/3	67%	1	100%	-	-
16	J01MA14	Moxifloxacin	-	-	-	-	1/12	8%	-	-	-	-	-	-	-	-

(-) Gram-Negative bacteria; (+) Gram-Positive bacteria

elderly patients are more prone to pneumonia infection due to the disturbance of gag reflex, weakening of immunity, disruption of thermoregulation, and multiple degrees of cardiopulmonary abnormalities [11].

In this study, the most used antibiotic was intravenous ceftriaxone. A similar study by Anindia (2016) at Airlangga University Hospital showed that ceftriaxone was the most commonly used antibiotic [10]. Antibiotic choices available

for pneumonia patients are beta-lactam combined with intravenous anti-beta lactamase or the second and the third generation of intravenous cephalosporin, or intravenous respiratory fluoroquinolone. Mostly used antibiotic is ceftriaxone, which is the third generation cephalosporin with wide spectrum effectivity. Ceftriaxone has an advantage as compared to other cheaper third generation cephalosporins since there is no need for dose adjustment in patients with renal malfunction, longer half-life that enables once-daily dose, and least possibility of allergy. The mechanism of ceftriaxone inhibits bacterial cell wall synthesis by binding one or more of the penicillin-binding proteins (PBP) that inhibit the last step of transpeptidase to synthesize peptidoglycan on bacterial cell wall. Ceftriaxone is a broad-spectrum antibiotic that is effective in dealing with most aerobic organisms, either Gram-positive or Gram-negative. Ceftriaxone is also more susceptible to Enterobacteriaceae, which is beta-lactamase producing strain.

In this study, the most used antibiotic in pneumonia patients was the combination of ceftriaxone and levofloxacin. Based on the pneumonia guidelines, the combinations of antibiotics can be given to inpatients without modification factors since the combinations are intravenous beta-lactam altogether with anti-beta lactamase, or second and third generation of cephalosporin, or intravenous respiratory fluoroquinolone. Pneumonia patients with modification factor received the second and third generations of intravenous cephalosporin. Meanwhile, if atypical bacterial infection occurs, a new group of macrolides is administered. If there is no risk of pseudomonas infection, the third generation of cephalosporin can be combined with macrolide or fluoroquinolone.

The culture of 74 patients showed 17 types of bacteria, consisting of five Gram-positive bacteria and twelve Gram-negative bacteria. Based on the culture result, the most common causes of pneumonia were *Streptococcus viridans* found in 18 patients (22.5%), *Acinetobacter baumannii* in 12 patients (15%), and *Klebsiella pneumoniae* in 12 patients (15%). The finding is different from the previous study which stated that the most common bacteria were *Pseudomonas aeruginosa*, *Staphylococcus coagulase negative*, and *Streptococcus viridans* [10]. It also differs from another study by Mudatsir (2012) conducted in Dr. Zainoel Abidin General Hospital in Banda Aceh, which stated that the most common bacteria were *Klebsiella pneumoniae* (38.6%), *Pseudomonas aeruginosa* (18.1%) and *Acinetobacter spp* (18.1%) [13]. Multicenter data from hospitals in Indonesia in 2012 showed that the most common cause of pneumonia from sputum analysis is Gram-negative bacteria, such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, whereas Gram-positive bacteria, like *Streptococcus pneumoniae*, *Streptococcus viridans*, *Staphylococcus aureus* are found only in small amount [2]. This culture result raises some concerns about a difficult therapy against Gram-negative bacteria, including bacterial resistance [14-17]. In addition, this result can affect the empirical antibiotic therapy regimens by where the antibiotics may become sensitive,

intermediate, or resistant. However, according to the Ministry of Health of the Republic of Indonesia, empirical antibiotic therapy has to be prescribed based on the surveillance data of pathogen in local hospitals [18].

Based on the quality of antibiotic use concerning Gyssens method, 37 patients (50%) received antibiotics wisely. The knowledge regarding rationale of antibiotic therapy consists of two important evaluative aspects. The aspects include: first, quantity - the number of antibiotics given, and second, quality - the precision in choosing the type of antibiotics, dosage, and lengths of therapy. The quality of antibiotic therapy is assessed based on patients' medical records.

In IVC category, there are other cheaper types of antibiotics with the frequency of 19 (24.68%), such as the administration of intravenous levofloxacin administration of 750 mg every 24 hours. The selected antibiotics for pneumonia are beta-lactam and anti-beta lactamase or the third generation of cephalosporin. Ceftriaxone is the cheaper version of the third generation of cephalosporin compared to levofloxacin which is a fluoroquinolone and according to Gyssens analysis is included in the IVC category. In IIIA category, there is an overuse of antibiotic with a frequency of 6 (7.79%). Based on the data from IDSA/ATS/BTS, the use of antibiotics for pneumonia can range from 24 hours to 14 days with the antibiotic sensitivity evaluation and patient clinical condition. The result of this study indicates that there are some antibiotics given in more than 14 days without evaluation of its effectivity. In IIIB category, too short the use of antibiotics with a frequency of 15 (19.48%) with mean of the use between 24 and 72 hours. This situation occurs when a patient is referred from another hospital, experiences complications of the secondary disease, or death.

Antibiotic quality with a good score indicates the prudent use of an antibiotic. The administration is not only empirical but also definitive according to the bacterial antibiotic sensitivity testing. This result test needs to be accompanied with the recommendation of selected antibiotics after considering the clinical relevance of the patient. Microbial examination altogether with clinical conditions is important to perform surveillance, preventive and curative (treat infectious diseases), and control infections in hospitals, health care facilities, and community.

CONCLUSION

The microbial profile in pneumonia patients admitted to the pulmonology ward in Dr. Soetomo General Hospital was dominated with Gram-negative bacteria. The most common Gram-negative species was *Acinetobacter baumannii*, followed by *Klebsiella pneumoniae*. In contrast, the most common Gram-positive bacteria was *Streptococcus viridans*. The total of the antibiotics used was 35.53 DDD per 100 bed days, and the mostly used antibiotic was ceftriaxone with 9.23 DDD per 100 bed days. Based on Gyssens method, half of the antibiotics used in pneumonia patients were appropriate.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study has been approved by the Health Research Ethics Committee of RSUD Dr. Soetomo General Hospital, Surabaya, Indonesia under approval no. 0061/KEPL/II/2018.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013 (<http://ethics.iit.edu/ecodes/node/3931>).

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available in the Ubaya repository at http://digilib.ubaya.ac.id/data_pustaka-251604.html

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

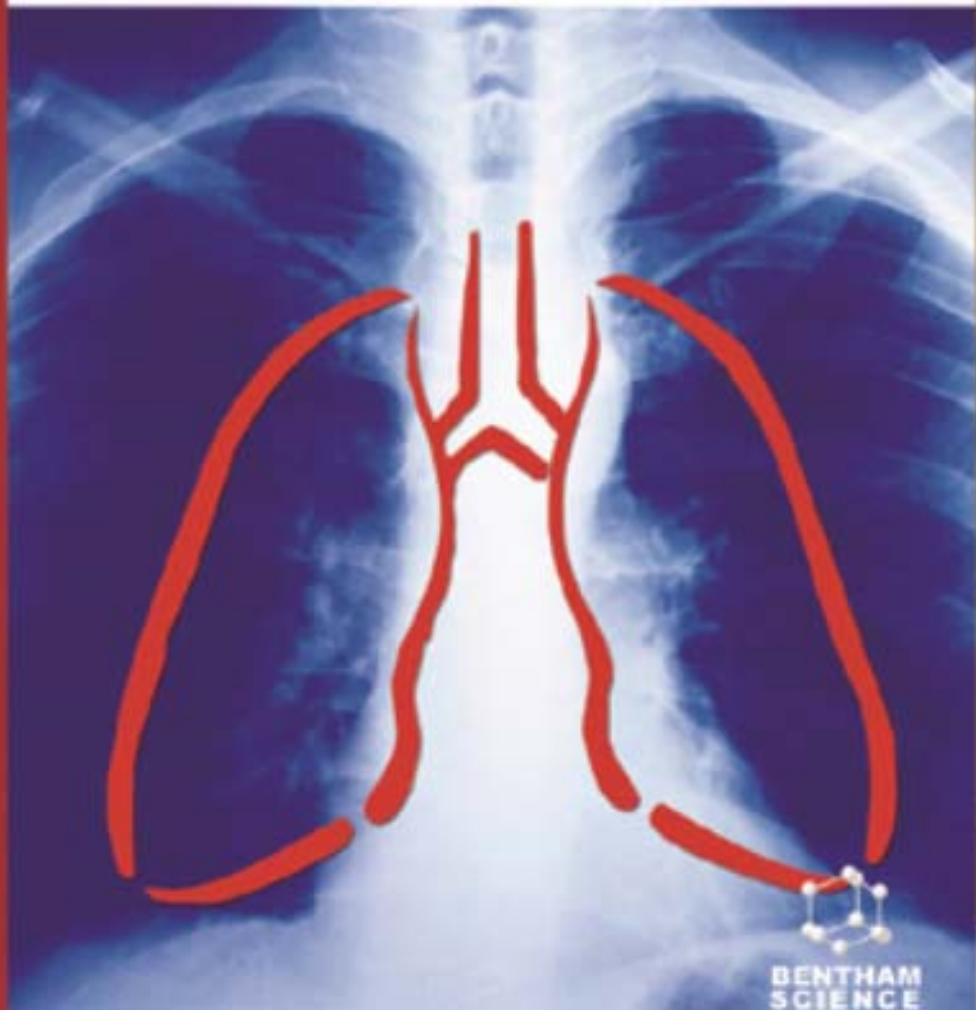
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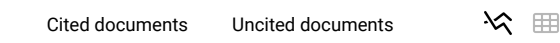
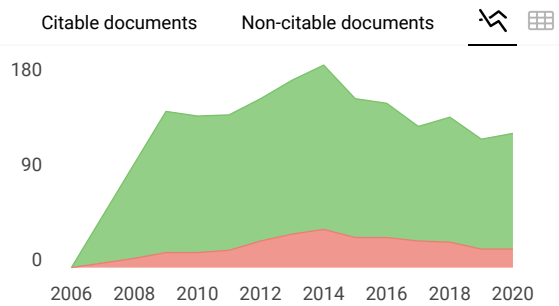
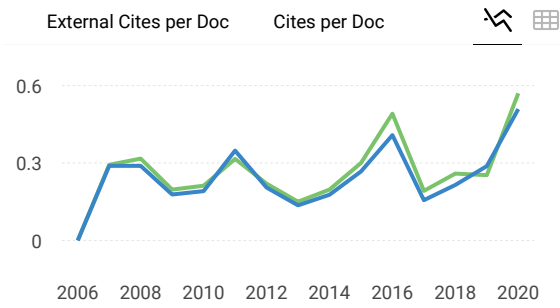
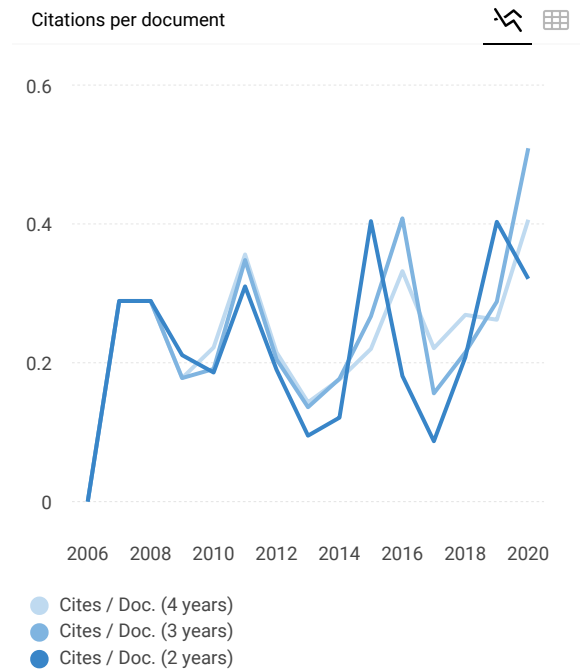
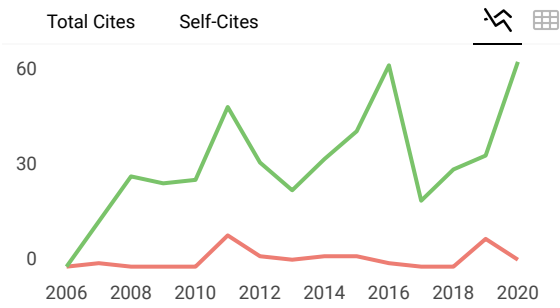
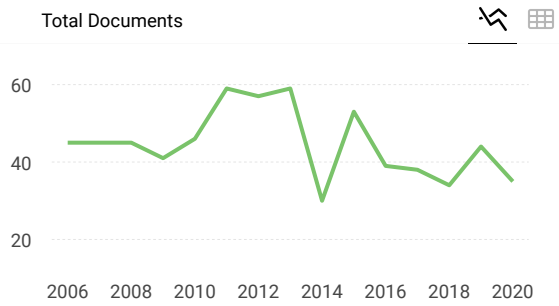
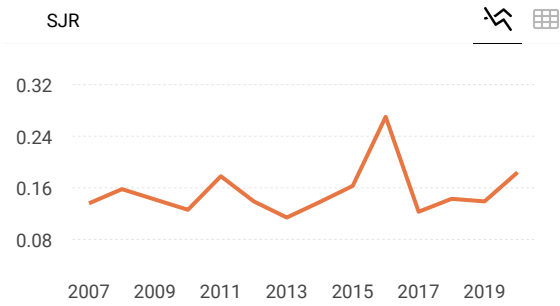
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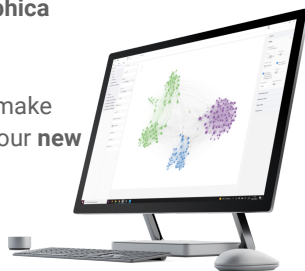
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Article List

Meet Our Editorial Board Member

[Vol. 16 , Issue. 1]

Author(s): Caterina Ledda

Pages: 1-2 (2)

Free

Coronavirus in the Arena: One More Time

[Vol. 16 , Issue. 1]

Author(s): Abbas Alshami, Steven Douedi and Joseph Varon

Pages: 3-4 (2)

Free

Landmark Studies of Targeted Therapies for Advanced Non-Small Cell Lung Cancer: A Guide for Pulmonologists

[Vol. 16 , Issue. 1]

Author(s): Adrien Costantini, Theodoros Katsikas and Clementine Bostantzoglou*

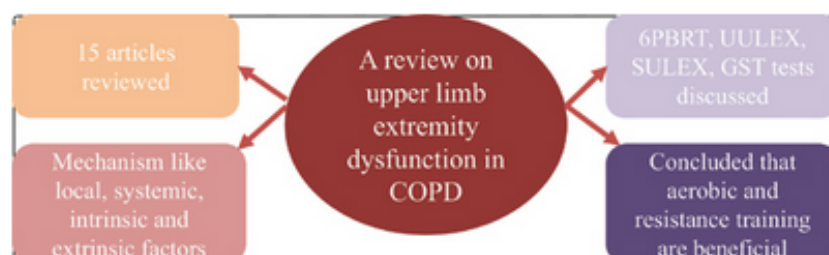
Pages: 5-10 (6)

Upper Limb Extremity Muscle-Dysfunction in Chronic Obstructive Pulmonary Disease: A Narrative Review

[Vol. 16 , Issue. 1]

Author(s): Kulkarni M. Suhas, Gopala K. Alaparathi*, Shyam K. Krishnan and Kalyana C. Bairapareddy

Pages: 11-20 (10)



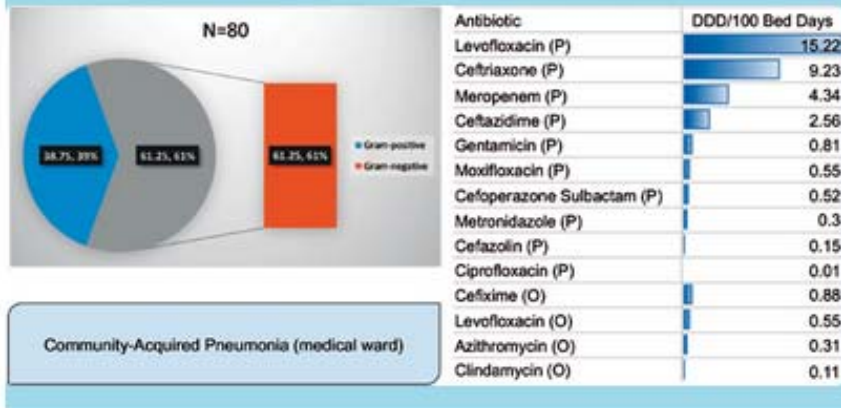
Bacterial Profile and Antibiotic Use in Pneumonia Patients at Dr. Soetomo General Hospital

[Vol. 16 , Issue. 1]

Author(s): Rika Yulia, Josephine Witha Mariza, Soedarsono and Fauna Herawati*

Pages: 21-27 (7)

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Creatinuria and Dynamics of Calcium Metabolism in Children in the Phase of Exacerbation of Bronchial Asthma

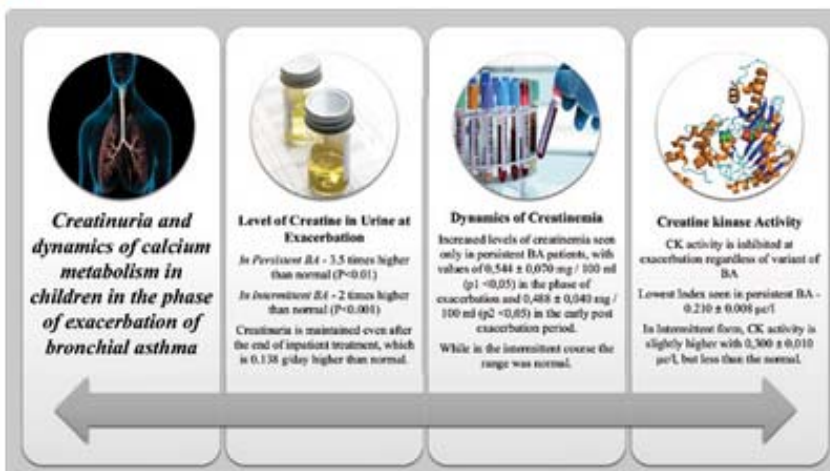
[Vol. 16 , Issue. 1]

Author(s): Vitalii B. Kaliberdenko , Shanmugaraj Kulanthaivel*, Michael V. Shterenhis, Olga Y. Poleshchuk, Kadri Mametov ,

Lutfie Mametova and Keerthanaa Balasundaram

Pages: 28-33 (6)

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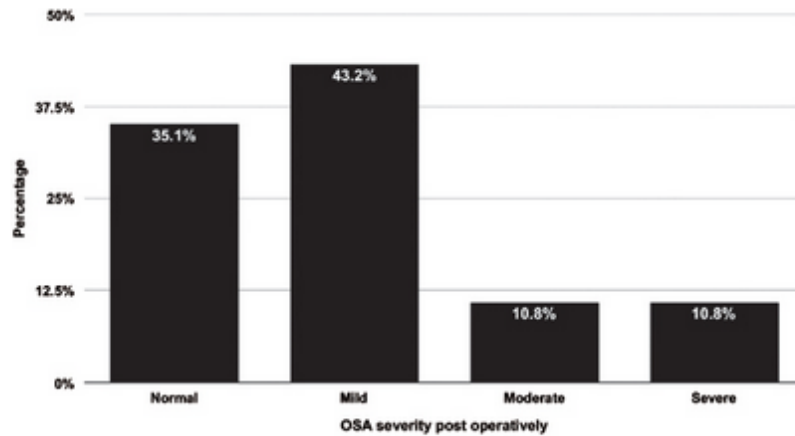


Long-term Effects of Gastric Bypass Surgery in Patients with Obstructive Sleep Apnea

[Vol. 16 , Issue. 1]

Author(s): Nathir Obeidat, Saif Aldeen AlRyalat*, Khaled Al Oweidat, Mahmoud Abu-Khalaf, Asma Btoush, Mohammad Al-Essa, Zaina Obeidat, Mohammed Obeidat and Ayman Wahbeh

Pages: 34-38 (5)

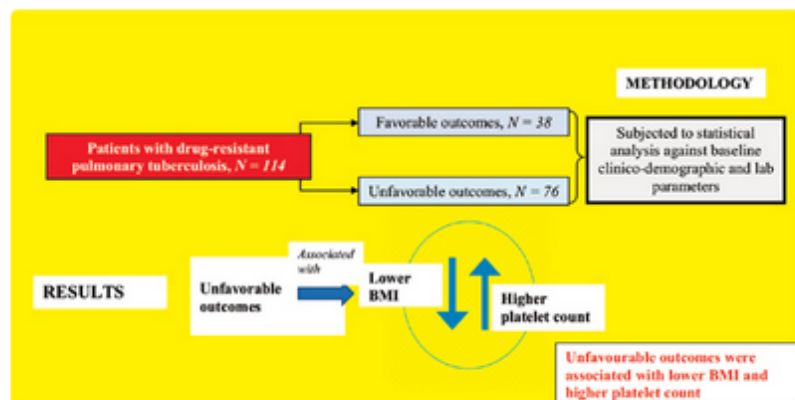


Association of the Clinico-Demographic and Laboratory Profile with Treatment Outcomes in Patients with Drug-Resistant Pulmonary Tuberculosis

[Vol. 16 , Issue. 1]

Author(s): Alam Nawaz, Manel Arjun Nayak*, Samarth Mahadevappa and Ashwin Kamath

Pages: 39-46 (8)

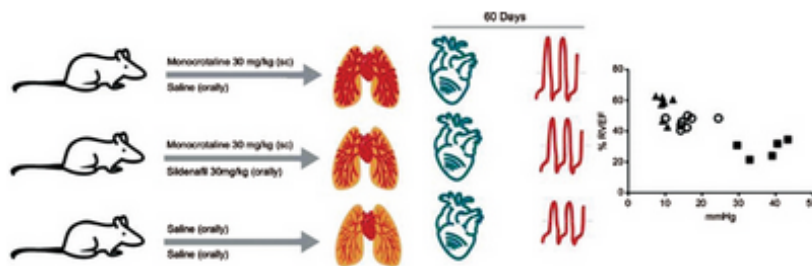


Relationship between Invasive and Non-Invasive Hemodynamic Measures in Experimental Pulmonary Hypertension

[Vol. 16 , Issue. 1]

Author(s): Vicente Benavides-Córdoba* and Mauricio Palacios Gómez

Pages: 47-53 (7)

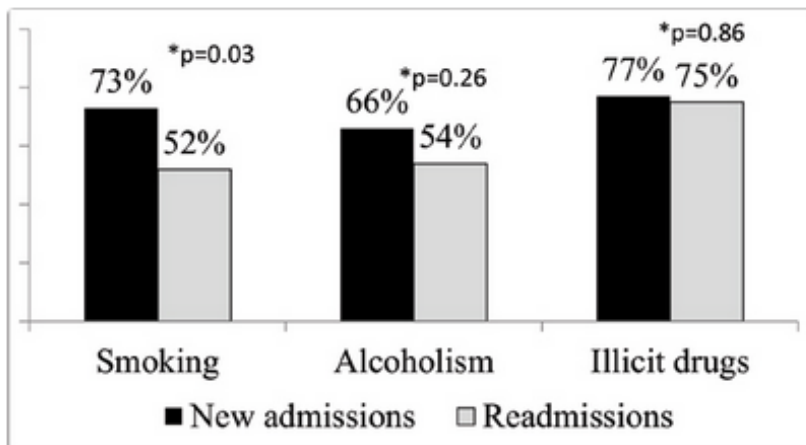


Early Hospital Readmission in Patients With Tuberculosis: Social and Cultural Risk Factors

[Vol. 16 , Issue. 1]

Author(s): Diana M. Valenzuela-Soltero, Jesús A. Güereca-Alvarado, Murielle Pacheco-Barajas, Nathaly Sánchez-Rebollar and Rafael Laniado-Laborín *

Pages: 54-58 (5)




Vitamin D among Patients of Pulmonary and Extrapulmonary Tuberculosis: A Prospective Case-control Study

[Vol. 16 , Issue. 1]

Author(s): Doaa Gadallah*, Ahmed Sedky and Hend Mohamed Esmaeel


Pages: 59-65 (7)

Background: People with vitamin D deficiency are highly liable to develop active pulmonary and extrapulmonary tuberculosis



Vitamin D

Patients and methods: A case-control prospective study was conducted among patients with pulmonary and extra pulmonary tuberculosis and asymptomatic persons. **Results:** Study revealed that 52 patients were vitamin D deficient, 7 patients had insufficient vitamin D and 21 had normal serum level. Of the extrapulmonary TB patients, 35 (100%) had vitamin D deficiency, in pulmonary TB patients, 15 (100%) were vitamin D deficient. While, 2 study subjects (6.7%) in the control group were deficient of vitamin D, 7 (23.3%) had insufficient vitamin D and 21 cases had normal vitamin D level.



Conclusion: Vitamin D deficiency was found among pulmonary and extrapulmonary tuberculosis patients especially among female patients and rural residence. The current study needs additional work to evaluate the value of adding of vitamin D to the TB treatment regimen.

Vitamin D deficiency among pulmonary and extrapulmonary tuberculosis patients

Asthma-COPD Overlap (ACO) among Adult-onset Asthma Patients

[Vol. 16 , Issue. 1]

Author(s): Daniel Maranatha* and Nurkristi Permatasari Amin

Pages: 66-70 (5)

