Risk Factor Analysis and Outcomes of VAP in ICU Patients at Arifin Achmad General Hospital in 2018: Cohort Retrospective Study

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Abstract: Ventilator associated pneumonia (VAP) is a nosocomial pneumonia that occurs 48 hours or more after mechanical ventilator usage through the endotracheal tube or the tracheostomy tube. VAP is one of the nosocomial infections often found in the intensive care unit (ICU). The purpose of this study was to determine the risk factors and outcomes of VAP. This study used a retrospective cohort design involving all ICU patients at Arifin Achmad General Hospital in 2018 who met the inclusion criteria. The incidence of VAP was 3.1% (95% CI 2.76 - 3.43). The onset of VAP that occurred within 5 days was 66.7%. A significant factor was history of pulmonary disease (p = 0.04) with an RR of 8.2 (95% CI 1.7 - 40.1). There was a significant correlation between the incidence of VAP and length of ICU stay (p = 0.002). The incidence of VAP in Arifin Achmad General Hospital in 2018 was 3.1%. The onset of VAP incidence is still within 5 days, so the prognosis is still good. Doctors and paramedics should pay more attention to ICU patients who have a history of pulmonary disease.

1 INTRODUCTION

The incidence of pneumonia after mechanical ventilation usage increases 3–10 times (Augustyn, 2007), and may causes nosocomial pneumonia if its usage is more than 48 hours, either with endotracheal tubes or after tracheostomy and is called Ventilator-Associated Pneumonia (VAP) (Hunter, 2005; Patricia , Dorrie, & Barbara, 2012)

Ventilator Associated Pneumonia (VAP) causes an increase in morbidity and mortality of patients that were treated in The Intensive Care Unit (ICU) (Kahlil, 2017)

The incidence of VAP is quite high, varying between 9-27% with a mortality rate of more than 50%. The incidence of VAP in Cipto Mangunkusumo Hospital (RSCM) was 27.4% with a mortality rate of 57.2% (Saragih, 2014). At Pamukkale University Hospital, Denizli, Turkey for 38.1% with a mortality rate of 70.3% (Erbay, 2004). VAP data on patients treated in the ICU and CVCU rooms at Arifin Achmad General Hospital in Riau Province was increasing from 3.3% in 2013 to 18.58% in 2015 (Nency, 2015).

There are two risk factors that may increase the incidence of VAP, they were intervention factors and patient factors. Intervention factors include endotracheal intubation, duration of use of mechanical ventilation, length of hospital stay, use of Endotracheal Tube (ETT), catheters, central venous pressure measurement, inappropriate use of antibiotics, red blood cell transfusion, supine position, and post-surgery.While the patient factors include age over 60 years, gender, and Chronic Obstructive Pulmonary Disease (COPD) (Gillepspie, 2009).

According to Saragih (2014), research on VAP in Indonesia has not been comprehensive. Most of the patients were lack of knowledge in VAP and do not have health insurance, so they were admitted in severe conditions. This resulted in more frequent occurrences of VAP. VAP is one of the causes of morbidity and mortality in ICU but also causes the prolonging of the patient stay which may result in the increasing cost of treatment (Wiryana, 20007).

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This study was to determine the risk factors and outcomes of VAP in ICU patients at Arifin Achmad General Hospital during 2018.

2 METHODS

This study was an analytical study with a retrospective cohort design. General and clinical data during treatment were obtained from the register book. The study was conducted in March 2019 at Arifin Achmad General Hospital in Riau Province. The population in this study were all data on patients using mechanical ventilators who were admitted to the ICU in January-December 2018. The samples in this study were all of the populations that met the inclusion criteria using a total sampling technique.

The inclusion criteria in this study were all patients who used mechanical ventilators for more than 48 hours in the ICU and had complete data (age, sex, postoperative procedure, history of pulmonary disease (COPD, Lung Ca, asthma, Pneumonia, Pulmonary TB), onset VAP, outcome of VAP (death or life), and length of stay.

Data obtained from register books are processed using computer statistics programs. Univariate analysis was carried out descriptively by using frequency distribution tables and calculating percentages. While the bivariate analysis was carried out using the chi-square statistical test and the mean/median difference test. Occurrence risk is measured using the value of Relative Risk (RR).

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3 RESULTS

During the period January-December 2018, there were 456 ICU patients who were treated more than 2 days (48 hours). 259 of them used mechanical ventilators, but only 192 patients met the inclusion criteria. Demographic and clinical characteristics of the research subjects can be seen in table 1.

Table 1. Demographic and clinical characteristics of Arifin Achmad Hospital ICU patients in 2018.

Variable	Total	Percentage (%)
Age		
≥ 60 years	48	25
< 60 years	144	75
Gender		
Man	97	50,5
Woman	95	49,5
Post surgery		
Yes	139	72,4
Not	53	27,6
Pulmonary disease history		
Yes	11	5,7
Not	181	94,3

In this study, the average age of ICU patients was 52.5 years (19-85) years. Most were found at <60 years of age (75%). The result of this study is the same as the result of Nency's (2015) study at Arifin Achmad General Hospital and Salukanan (2017) at RSUP dr. Hasan Sadikin Bandung, each of whom found 76.2% and 77.1% of ICU patients aged <60 years.

ICU patients were found slightly more in men (50.5%) than women (49.5%). The resultof this study is the same as those of Saragih (2014) at RSCM, and Susmiarti (2015) in Rumkital, dr. Ramelan Surabaya, each of which found 53.7%, and 83.3% of ICU patients were male.

139 ICU patients were found after surgery (72.4%). Similarly, the result of the Ciginskiene study (2019) at Lithuanian University of Health Sciences found 38.3% after surgical intervention. And Turkovic's (2017) research result at the University Hospital Center in Zagreb, Croatia which found 72% of ICU patients before tracheotomy and 82% after tracheotomy after neurosurgical. The resultof the Salukanan study (2017) also found that 40% of ICU patients after post laparotomy for various reasons, 26.4% after post craniotomy for various reasons.

In this study, patients who did not have a history of lung disease were more than those who had a history of pulmonary disease,181 patients (94.3%). Similarly, Susanti's (2015) research result at Eka Hospital Pekanbaru and Abbasinia (2016) in Al-Zahra Hospital, Isfahan, Iran, each of which found 70% and 46.9% of ICU patients had no history of pulmonary disease.

Table 2. The incidence of Ventilator-associated pneumonia in ICU Arifin Achmad Hospital patients in 2018.

Category	N	%
VAP	6	3,1
Not VAP	186	96,9
Total	192	100

From table 2, it was found that of 192 patients admitted to the ICU, there were 6 patients suffered from VAP (3.1%). Similarly, Saragih's research result: 27.4%; Nency: 18.58%; Salukanan: 8.5% and Turkovic: 42%.

Table 3. Onset of The Incidence of Ventilator-Associated Pneumonia in ICU Patients at Arifin Achmad Hospital in 2018.

Ventilator associated pneumonia	N	%
• ≤ 5 days	4	66,6
• >5 days	2	33,4
Total	6	100

From table 3, it is known from 6 patients suffered from VAP, 4 patients experienced it in ≤ 5 days (66.6%). Similarly, the result of Nency's research: 95.2%; Saragih: 52.2%; Abbasinia (2016) in the ICU of Al-Zahra Hospital, Isfahan, Iran: 18.8% and Agustina (2018) in the RSUD Dr. Loekmono Kudus Hadi: 46.7%.

Table 4. Outputs for Arifin Achmad Hospital ICU patients in 2018.

Outcome	**N**	**%**
• Died	66	34,4
• Life	126	65,6
Total	192	100
Length of ICU stay (days)	(med,min-max)	
• VAP	12,5 (7 – 36)	
• Not VAP	4 (2 – 52)	

From table 4, it is known that from 192 patients admitted to the ICU, more patients lived than died. (65.6% vs 34.4%). The result of this study is the same as those of Turkovic (2017) who found that more patients lived than died. 65% before tracheotomy and 75% after tracheotomy. However, it is different from the result of Erbay (2004) in Pamukkale University Hospital, Denizli, Turkey, Saragih (2014) and Salukanan (2017), which found more patients died than living. Each of them was 70.3%, 57.2%, 60%.

The average length of ICU stay for VAP patients in this study was 12.5 (7-36) days. Similarly, the research result of Dewi (2014) at Dr. RSUP Kariadi Semarang found an average of 12.21 ± 9.578 days and Erbay (2004) 8 days.

Table 5. Bivariate Analysis of VAP Risk Factors.

	VAP		**Not VAP**		**P value**	**RR**
	N	%	n	%		
Age						
≥ 60 years	1	16,7	47	25,3	1	0,6
< 60 years	5	83,3	139	74,7		(0,072-5)
Genders						
Man	3	50	94	50,5	1	0,97
Woman	3	50	92	49,5		(0,203-4,73)
Post surgery						
Yes	4	66,7	135	72,6	0,669	0,76
Not	2	33,3	51	27,4		(0,144-4,04)
Pulmonary disease history						
Yes	2	33,3	9	4,8	0,04*	8,2
Not	4	66,7	177	95,2		(1,6-40,1)

* Pulmonary disease history: COPD, Lung Ca, asthma, Pneumonia, Pulmonary TB

Table 5 shows that pulmonary disease history is the only variable that has a significant difference in the incidence of VAP (p = 0.04). This is similar to the result of Saragih (2014) and Ibrahim (2000) at Barnes Jewish Hospital in St. Louis, MO, who found significant differences in patients with comorbidities, one of which was Chronic Obstructive Pulmonary Disease. While other variables such as age, gender and postoperative procedures did not show a significant difference with the incidence of VAP.

Table 6. VAP Outcome Bivariate Analysis.

	Died		Life		p value	RR
	N	%	n	%		95% CI
VAP						
Yes	3	50	3	50	0,415	1,47
Not	63	33,9	123	66,1	66,1	0,64 – 3,36

Table 6 shows that the proportion of VAP patients who died and lived was equal to 50% but did not show a significant difference. Similarly, the results of a study by Kahlil (2017) which found no significant difference (p = 0.662) in group I (60%) and group II (70%) deaths that shared a positive culture after 48 h of mechanical ventilatio.

Table 7. Differences in duration of care for ICU patients who experience VAP and not VAP.

	VAP	Not VAP	p value
Length of ICU stay (days) (med,min -max)	12,5 (7 – 36)	4 (2 – 52)	0,002*

Table 7 shows that the incidence of VAP showed a significant difference with the length of ICU stay of patients in the ICU (12.5 days). The results of the Turkovic (2017) study also found a significant difference in the length of stay of VAP patients before and after the tracheotomy, which was 5 (4-9) days to 11 (10-13) days with p = 0.001. Similarly, the Rello (2002) study found a greater number of ICU days (11.7 ± 11.0 days, p <0.001) and longer hospital length of stay (25.5 ± 22.8 days, p <0.001).

4 DISCUSSION

4.1 Age

In this study, the average age of ICU patients was 52.5 years (19-85) years. Most were found at <60 years of age (75%). The incidence of VAP was also more common at <60 years of age (83.3%) but was not significantly associated.

According to Smeltzer and Bare (2013) age is one of the factors that may affect a person's immune system which will affect someone's ability to react to microorganisms. In addition, an increase in age will also reduce the production and function of T and B lymphocytes and thus increase the incidence of autoimmune diseases. Therefore, the frequency and intensity of infections will increase in old age. It can be said that age <60 years or 60 years is equally at risk of VAP.

4.2 Gender

In this study, the comparison of male and female patients in ICU are similar (50.5% vs. 49.5%). The incidence of VAP was also similar in male and female patients (50% vs 50%) and was not significantly associated.

Pneumonia infection is more common in men than women because of the estrogen in women which can activate nitric oxide synthase-3 (NOS3) that can increase the activity of macrophages to kill infectious microbes (Lee, 2008 & Yang et al, 2014)

But according to Sukmadi (2018), patients admitted to the ICU are not always dominated by one sex either male or female.

4.3 Post Surgery

In this study, most ICU patients were patients who were treated after surgery (72.4%). VAP events were also more common in patients after surgery (66.7%) but were not significantly associated.

The results of the Cunnion study (1996) found more incidence of VAP in postoperative patients than non-surgical patients. Especially in patients after cardiothoracic surgery and head injury. This is due to low preoperative albumin levels, prolonged preoperative care and difficult surgical procedures.

According to Mc Carthy et al (2008) the installation of the endotracheal tube (ETT) and decreased consciousness due to anesthesia after surgery will reduce the patient's ability to swallow effectively and eliminate coughing which is the body's natural defense mechanism against respiratory tract infections. As a result, when microorganisms enter the lungs, the body's defense mechanism cannot kill the organism. In addition, esophageal reflux and aspiration of gastric contents in ETT patients can also cause endobronchial colonization and pneumonia.

4.4 Pulmonary Disease History

In this study, 94.3% of ICU patients had not a history of pulmonary disease (COPD, Lung Ca, asthma, Pneumonia, Pulmonary TB). 33.3% developed into VAP but were significantly associated (p value = 0.04).

Susanti's (2015) study found 30% of patients with pulmonary disease: COPD, respiratory failure and Acute Long Oedema (ALO) using a ventilator. When using a ventilator, the risk of being treated will be longer compared to patients who do not use a ventilator, and will increase the risk of suffering from VAP.

According to Price (2006), one lung disease that can cause pneumonia is COPD. Patients with COPD experience epithelial and ciliary damage in their respiratory tract. Because it is damaged, the production of goblet cells will increase. Goblet cells produce sputum which becomes a place for microbes to develop. This explains why pneumonia infection often occurs in acutely exacerbated COPD patients (Sogaard et al, 2016).

Pneumonia in COPD patients will increase pulmonary function disorders, increase hypoxemia and infection, resulting in systemic inflammation, sepsis to organ failure (Sogaard et al, 2016). Bronchitis and pneumonia are the most common hospital infections in ICUs Kahlil (2017).

4.5 VAP Incidence

The incidence of VAP in this study was only 3.1%. According to Agustyn (2007) the incidence of VAP in patients using mechanical ventilation was 22.8% and contributed to 86% of nosocomial infections. Whereas according to Turkovic (2017) the incidence of VAP in ICU which is reported as 15.5% and 9.3%. Chen et al's research in Taiwan found a VAP incidence of 3.18 per 1000 days of ventilator use and ranked second in the ICU.

The results of the Salukanan study (2017) found an incidence of VAP of 8.5 cases per 1,000 days of ventilator use. This figure is quite high, but it is still within tolerance in developing countries. Because the incidence of VAP in developing countries range from 1.2 to 8.5 per 1,000 days of ventilator use. Compare this with developed countries ranging from 0.2 to 4.4 per 1,000 days of ventilator use.

According to Amanullah and Posner (2010), 28% of complications of the patients who use mechanical ventilation cause VAP. The incidence is directly proportional to the duration of use of mechanical ventilation. Estimated incidence of 3% per day for the first 5 days, 2% per day for 6-10 days, and 1% per day after 10 days.

4.6 VAP Onset

The onset of VAP≤ 5 days in this study was 66.6%. According to Ibrahim (2000), in general, early onset VAP (≤ 5 days) has a better prognosis because germs are still sensitive to antibiotics. Conversely, late-onset VAP (> 5 days) has a worse prognosis because there has been colonization of Multi-Drug Resistant (MDR) bacteria so that the mortality rate will increase (Torres, 2004 & Nency, 2015)

4.7 Outcome

4.7.1 Died/Life

The number of ICU patients who died in this study was less than those living (34.4% vs. 65.6%). However, the number of VAP patients who died and lived was equal (50% vs. 50%), although it was not significantly related.

Some studies have found a relationship between death and VAP. These include the Turkovic (2017) case-control study in 85 VAP patients and 85 non VAP patients at the University Hospital Center in Zagreb, Croatia. He found 40% of deaths in VAP patients and 38.8% in non VAP patients. There were no significant differences between the two classifications.

The Fagon et al. Study, in 1.118 patients using mechanical ventilation, found an association between VAP and a one-and-a-half increase in the risk of death (odds ratio, 1.51; 95% CI, 1.11-2.03) (Safdar, 2005) .

According to Erbay (2004) the main cause of death from hospital-acquired infections is Nosocomial Pneumonia (NP). 25% of nosocomial infections in hospitals are distributed by patients admitted to the ICU. The cause of high nosocomial infections in the ICU is due to the patient's main diagnosis, the severity of the disease, the length of treatment and the invasive device used by the patient. The estimated prevalence of NP within the hospital settings ranges from 10% to 65%, with case fatality rates which is greater than 25% in most studies.

According to Saragih (2014) the high mortality rate of VAP in Indonesia besides due to improper use of antibiotics, also caused by the management is not optimal, which is caused by limited funds (66% of the research subjects have no health insurance).

4.7.2 Length of ICU Stay (days)

The average length of stay for VAP patients in this study was 12.5 (7-36) days. 3 times longer than the treatment of patients who were not diagnosed with VAP. The results of the analysis showed a

significant difference between the length of stay with the incidence of VAP (p-value: 0.002).

The results of the study by Kahlil (2017) found that the length of stay in the ICU was around 7-54 days. According to the study, VAP is an infection in a hospital that has an impact on the length of stay, increased hospital costs and a greater risk of death.

Turkovic (2017) also found that VAP patients were treated longer in the ICU than patients without VAP. Several studies report that patients with VAP have increased the length of stay and hospital costs (Safdar, 2005). Warren et al. (2003) reported that the cost of hospitalization for patients with VAP was significantly higher than for patients without VAP ($ 70,568 vs. $ 21,620). Rello (2002) found the average hospital bill for VAP patients to be $ 104,983 ± $ 91,080. Which is significantly bigger.

In addition Rello (2002) also found that patients with VAP had a significantly longer hospital length of stay (25.5 ± 22.8 days, p <0.001) and a greater number of ICU days (11.7 ± 11.0 days, p <0.001). The number of days of treatment for patients with VAP is longer than for patients without VAP. 9.6 days longer due to mechanical ventilation, 6.1 days longer in the ICU, and 11.5 days longer in the hospital. And the average hospital bill cost of VAP patients is $ 40,000, which is significantly higher than patients without VAP.

5 CONCLUSION

VAP study was as much as 3.1%. The onset of VAP found within 5 days 66.6%, it is expected that the prognosis will be better. This study showed that risk factors for pulmonary disease history were only 33.3% but were significantly associated with the incidence of VAP (p-value = 0.04, RR = 8.2 (1.6-40.1)). VAP occurrencewere significantly related with length of stay for patients in the ICU (p-value = 0.002), with a median of 12.5 (7-36) days.

From this study we concluded that VAP needs more attention to prevent its occurrence. As once diagnosed, it usually increases ICUs mortality rates and its potentially substantial attributable moretality rates.

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REFERENCES

Abbasinia M, Bahrami N, Bakhtiari S, Yazdannik A, Babaii A. 2016. The Effect of a Designed Respiratory Care Program on the Incidence of Ventilator-Associated Pneumonia: A Clinical Trial. Journal of Caring Sciences, 5(2) : 161-167.

Augustyn, B. 2007. Ventilator-associated pneumonia risk factors and prevention. Critical Care Nurse, 27(4) : 32-39.

Ciginskien A, Dambrauskien A, Rello J and Adukauskien D. 2019. Ventilator-Associated Pneumonia due to Drug-Resistant Acinetobacter baumannii: Risk Factors and Mortality Relation with Resistance Profiles, and Independent Predictors of In-Hospital Mortality. Medicina, 55, 49 : 1-13.

Dewi H, Harahap MS. 2014. Hubungan Usia Penderita Ventilator Associated Pneumonia Dengan Lama Rawat Inap Di ICU RSUP Dr. Kariadi Semarang. Jurnal Media Medika Muda : 1-14.

Erbay RH, Yalcin AN, Zencir M, Serin S, Atalay H. 2004. Costs and risk factors for ventilator-associated pneumonia in a Turkish University Hospital's Intensive Care Unit: A case-control study. BMC Pulmonary Medicine 4 : 1-7.

Gillespie, R., 2009. Prevention and Management of Ventilator-Associated Pneumonia – The Care Bundle Approach, (Online), available from (http://ajol.info/index.php., 15th march 2019).

Ibrahim EH, Ward S, Sherman G, Kollef MH. 2000. A comparative anlysis of patients with early-oset vs late-onset nosocomial pneumonia in the ICU setting. Chest 117 : 1434-42.

Kahlil, NH , Khalil AT , Abdelaal DE. 2017. Comparison study between bacteriological aetiology and outcome of VAT & VAP. Egyptian Journal of chest Diseases and Tuberculosis 66 : 169-174.

Hunter JD. 2006. Ventilator associated pneumonia. Postgrad Med J 82 (965) : 172-8.

McCarthy, S.O, et al., 2008. Ventilator Associated Pneumonia Bundled Strategies; An Evidence-Based Practice. Worldview on Evidence-Based Nursing fourth quarter : 193–204.

Nency C, Irawan D, Andrini F. 2015. Gambaran Kejadian Ventilator-Associated Pneumonia Pada Pasien Yang Dirawat Di ICU Dan CVCU RSUD Arifin Achmad Periode Januari 2013 S/D Agustus 2014. JOM FK Volume 2 No. 2 Oktober 2015 : 1-9.

Patricia, G., Dorrie, F., & Barbara, M. 2012. Keperawatan kritis pendekatan asuhan holistik: Jakarta: EGC.

Price, A. 2006. Patofisiologi konsep kilinis proses-proses penyakit. Jakarta: EGC.

Rello J, et al. 2002. VAP Outcomes Scientific Advisory Group. Epidemiology and outcomes of ventilator-

associated pneumonia in a large US database. Chest 122 : 2115-2121.

Safdar N, Dezfulian C, Collard HR, Saint S. 2005. Clinical And Economic Consequences Of Ventilator-Associated Pneumonia: A Systematic Review. Crit Care Med 2005 Vol. 33, No. 10 : 2184-2193.

Saragih RJ, Amin Z, Soedono R, Pitoyo CW, Rumende CM. 2014. Prediktor mortalitas pasien dengan ventilator-associated pneumonia di RS Cipto Mengunkusumo. Departemen Anestesiologi dan Perawatan Intensif FK UI: Vol.2 No.2.

Salukanan RT, Zulfariansyah A, Sitanggang RH. 2018. Pola Pneumonia Nosokomial di Unit Perawatan Intensif Rumah Sakit Umum Pusat Dr. Hasan Sadikin Bandung Periode Januari–Desember 2017. JAP, Volume 6 Nomor 2, Agustus 2018 : 126-136.

Smeltzer, Bare SC, Brenda. G, 2013. Buku Ajar Keperawatan Medikal Bedah Brunner & Suddarth. Ed.8. Vol. 3. Jakarta: EGC :1698 – 1700.

Sukmadi A, Pujiastuti SE, Santjaka A, Supriyadi. 2018. Effectiveness Of Suction Above Cuff Endotracheal Tube In Preventing Ventilator Associated Pneumonia In Critical Patients In Intensive Care Unit. Belitung Nursing Journal. 2018 August; 4 (4) : 380-389.

Susmiarti D, Harmayetty, Dewi YS. 2015. Intervensi Vap Bundle Dalam Pencegahan Ventilator Associated Pneumonia (Vap) Pada Pasien Dengan Ventilasi Mekanis (The Incidence of VAP after VAP Bundle Intervention Among Patients with Mechanical Ventilation). Jurnal Ners Vol. 10 No. 1 April 2015 : 138–146.

Susanti E , Utomo W , Dewi YI. 2004. Identifikasi Faktor Resiko Kejadian Infeksi Nosokomial Pneumonia Pada Pasien Yang Terpasang Ventilator Di Ruang Intensive Care. JOM Vol 2 No 1, Februari 2015 590 : 590-599.

Torres A, Ewig S. 2004. Diagnosing ventilator associated pneumonia. N Engl J Med 2004. 350 : 433-522.

Turković TM, Obraz M, Glogoški MZ, Juranić I, Bodulica B, Kovačić J. 2017. Incidence, Etiology And Outcome Of Ventilator-Associated Pneumonia In Patients With Percutaneous Tracheotomy. Acta Clin Croat, Vol. 56, No.1, 2017: 99-109.

Warren DK, Shukla SJ, Olsen MA, Kollef MH, Hollenbeak CS, Cox MJ, Cohen MM, Fraser VJ. 2003. Outcome and attributable cost of ventilator-associated pneumonia among intensive care unit patients in a suburban medical center. Crit Care Med 2003, 31:1312-1317.

Wiryana, M. 2007. Ventilator Associated Pneumonia. J Peny Dalam, Volume 8 Nomor 3 Bulan September; 2007 : 254-268.