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# MONITORING OF SIDE EFFECTS OF ANTI-TUBERCULOSIS DRUGS ON THE CASES OF PULMONARY TB PATIENT IN CIKAMPEK PRIVATE HOSPITAL

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***Abstract---****In Indonesia Tuberculosis (TB) is still a serious health problem and shows an increase in cases from year to year. West Java (0.7%) province with the highest pulmonary TB, given the increasing drug-related problems (Drug Related Problems) against antituberculosis drugs in the category of adverse drug reactions (Adverse Drug Reactins). This study aims to obtain information on the side effects of antituberculosis drugs experienced by patients with new cases of pulmonary TB in Cikampek Private Hospital. The research method is a prospective observational monitoring of drug side effects on a regular basis every week for 1 month of intensive treatment. The number of samples in this study were 83 patients. The results showed that the percentage of side effects of antituberculosis drugs experienced by TB sufferers during intensive treatment were red in the urine (100%), nausea (34.85%), spasms (27.27%), tingling (18.18%) , dizziness (25.76%) and no appetite (15.15%). Fisher's test analysis results showed that statistically the socio-demographic characteristics of the respondents evaluated did not affect the incidence of ADRs, but clinically there was a significant relationship.*

***Keywords---****Mycobacterium tuberculosis, pulmonary TB, Drug Side Effects*

## I. INTRODUCTION

Based on data from the Health Ministry's Basic Health Research (RISKESDAS) in 2013, the prevalence of Indonesian population diagnosed with pulmonary TB by health workers in 2013 was 0.4 percent, not different from 2007. The five provinces with the highest pulmonary TB are West Java (0.7%), Papua ( 0.6%), DKI Jakarta (0.6%), Gorontalo (0.5%), Banten (0.4%) and West Papua (0.4%). The Health Profile of West Java Province in 2012 shows the data of TB sufferers in Karawang Regency with 2,821 new cases, 42 old cases with a prevalence of 129 cases per 100,000 population. One key to the success of TB treatment is patient compliance. Patients with TB who are not compliant with treatment are most likely due to long-term drug use, side effects that may arise, and lack of awareness of patients with the disease.

Drug-related problems or in clinical terms called DRPs (Drug Related Problems) are undesirable occurrences of patients related to drug therapy. Adverse drug reactions are an important part of drug related problems. ADR (Adverse Drug Reaction) is defined by WHO as a number of responses to dangerous and undesirable drugs, where it occurs at doses normally used in humans for prophylaxis, diagnosis, treatment of disease, or for modification of physiological functions.

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According to the mechanism ADRs are divided into two types namely type A and type B (Bent & Egherts. 2007, Lee (Ed). 2001).

Tuberculosis therapy requires a long therapy period of at least six months, so it is important to evaluate ADRs against anti-tuberculosis drugs (ATD). The implications of the occurrence of ADRs can result in decreased efficacy, Mycobacterium tuberculosis resistance, and therapeutic failure. The undesirable effect of the drug is the most likely cause for the patient to stop treatment. Singh & Pant, 2014 reported 38% of patients stopped treatment because of the effects of undesirable drugs. Including the decreased level of patient compliance in therapy as reported by Widjanarko et al., 2009, although the ADRs factor is not the only reason.

The socio-demographic characteristics of patients are often associated with tuberculosis and the incidence of anti-tuberculosis drug ADRs. Research by Suharjo & Girsang, M. (2015) concluded that tuberculosis is closely related to demographic factors including age group, sex, education, occupation and residence. The results of the analysis show that the risk factors for TB in Central Java are education level and employment status. The group of women who did not complete primary school had a higher risk of contracting TB compared to the group with higher education. In addition, the group of women who work tends to be at risk of TB compared to the group of women who do not work. While the study of the side effects of ATD in the PPTI Lung Clinic of DKI Jakarta region from January 1 2014 to March 2016 showed that age, sex, smear (+) and history of TB treatment were factors associated with the incidence of mild ESO and severe ESO (Reni, Wahyono , Yulismar, 2016). In the study of Marra et al. (2017) that female sex, increasing age, increased early AST, and drug resistance were associated with an increased incidence of ADRs. While the incidence of ADRs to ATD, especially primary ATD shows a very high number. An example can be seen in the studies of Gholami, Kamali, Hajiabdolbagh, Shalviri, (2006), where among 83 patients evaluated 44 (53%) patients showed at least one adverse reaction.

Another study conducted by Kurniawati, F. et al. (2012) on the ADRs incidence of primary ATD use in Penang General Hospital, Malaysia, showed that of 653 patients, there were 103 (15.8%) patients who showed adverse drug reactions. The majority of cases of adverse drug reactions were skin reactions in 51 (7.8%), hepatotoxicity of 17 (2.6%) patients, gastrointestinal reactions16 (2.5%) patients.

Research Athira et al. (2015) showed that out of 511 TB patients 93 (18.20%) experienced side effects of OAT. Diabetes mellitus (41.02%) is the most common comorbidity. Most ADR occurred in the intensive phase (85.71%) of treatment. Pulmonary TB (55.18%) is more common than extra-pulmonary TB. The majority of adverse drug reactions namely in gastrointestinal (GI) disorders (38.09%). The most serious ADR is hepatitis. Isoniazid is the main drug that causes 34.40% of unwanted drug reactions.

A pharmacovigilance study of ADRs on the use of first-line OAT in TB patients showed that approximately 58.87% of patients experienced ADR during the study period. Most ADR is due to isoniazid and rifampicin. Most serious side effects are hepatitis. (Honnaddi et al, (2016).

Research Abbas Akhmadi et al, (2017) about monitoring the Side Effects of Anti-Tuberculosis Drugs (ATD) in the Intensive Treatment Stage of Lung TB Patients in Makassar City in March-August 2015 showed the types of side effects experienced were 81% joint pain, nausea 79, 3%, itching 77.6%, lack of appetite 75.9%, dizziness 67.2%, tingling 50%, vomiting 41.4%, abdominal pain 34.5%, visual impairment 27.6%, pain head 24.1% and hearing loss 6.9%.

Considering the increasing cases of tuberculosis and the fact of primary antituberculosis drug DRPs in the category of Adverse Drug Reactions (ADRs), to improve the efficacy of treatment and improve the quality of life of patients, it is

necessary to conduct research to obtain information on the side effects of using primary anti-tuberculosis drugs (ATD) in patients with pulmonary tuberculosis a new case at the Cikampek Private Hospital.

## II. RESEARCH METHODS

This type of research is a prospective observational study with monitoring of patient side effects on a regular basis every week for 1 month of intensive treatment. This study was conducted at the Cikampek Private Hospital. The variables studied included: tingling, abdominal pain, no appetite, nausea, vomiting, dizziness, headache, itching, joint pain, spasms, visual disturbances, redness in urine and hearing loss. The population used in this study were all patients with pulmonary TB who seek treatment at the Cikampek Private Hospital, while the samples in this study were new cases of pulmonary TB patients undergoing antituberculosis drug treatment for a maximum of 1 month, age ≥ 18 years, and willing to be a response research.

The sampling technique used in this study was purposive sampling where each patient who came for treatment at the Cikampek Private Hospital and met the criteria for inclusion. The data collected is secondary data and primary data. Secondary data related to patient identity was obtained in the medical record, while primary data about the side effects of ATD experienced by TB patients were obtained through periodic interviews every week for 1 month of intensive treatment. Data analysis used univariate analysis to describe the percentage of side effects experienced by patients during intensive treatment and was presented through frequency distribution tables and graphs. The instrument used in data collection is the data search sheet (Data Collection Sheet).

## III. RESEARCH RESULT

Based on data from table 1 shows that, the percentage of tuberculosis patients is more in the age group 18-35 years 55.42% and the lowest is the age group> 54 years 5.1%. The proportion of sufferers was more in the female sex at 51.81% compared to the male sex at 48.19%. Based on the level of education, the percentage of sufferers was more at the level of high school education (63.86%) and elementary school as much as 18.07%, while the lowest percentage at the undergraduate level was 0.06%. Most new lung tuberculosis cases (43.37%) work as laborers / employees and only 0.04% as retirees.

Table 1. Distribution of Characteristics of New Case Lung TB Patients at Cikampek Private Hospital

| Demographic Characteristics | | | N=83(%) |
|---|---|---|---|
| Age | Productive | 18-35 years | 46(55,42) |
| | | 36-54 years | 15(18,07) |
| | Non prductive | >54 years | 22 (26,51) |
| Gender | | Women | 43(51,81) |
| | | Man | 40(48,19) |
| Employment | Work | Employee | 5 ( 0,06) |
| | | Enterpreneur | 29(34,94) |
| | | Labor | 36(43,37) |
| | No job | Pensionary | 3 ( 0,04) |

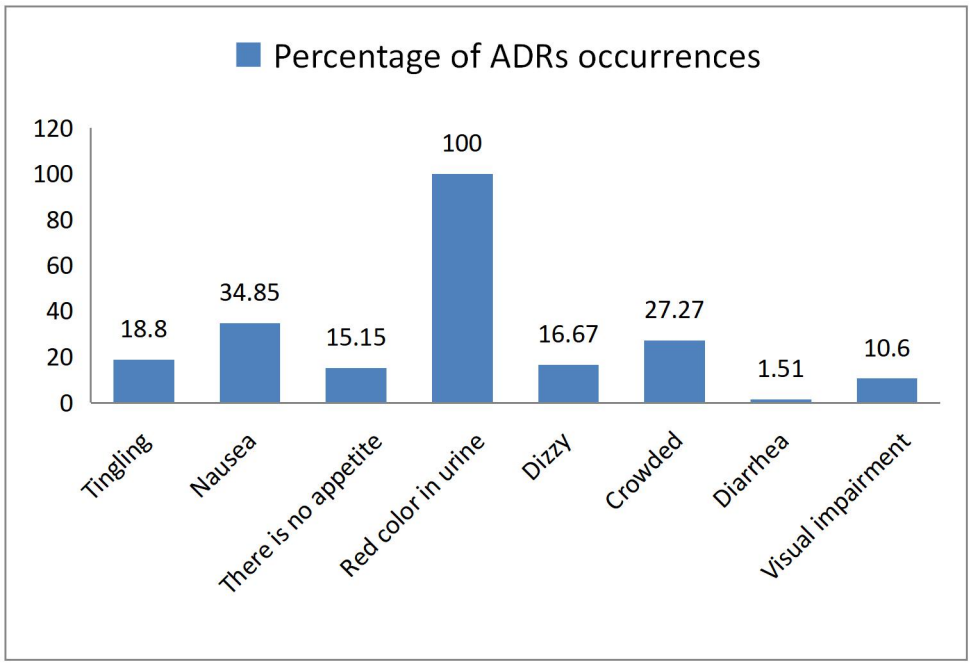
| Demographic Characteristics | | | N=83(%) |
|---|---|---|---|
| | | No job | 10( 0,12) |
| Education | Basic education | SD | 15(18,07) |
| | | SMP | 4 ( 0,05) |
| | Higher education | SMA | 53(63,86) |
| | | D3 | 6 ( 0,07) |
| | | S1 | 5 ( 0,06) |

N: Number of patients

Source: Primary Data

The percentage of patients who experience side effects of antituberculosis drugs is greater in the first and second week. The percentage of patients who experience side effects of antituberculosis drugs decreases with the passage of treatment.

Figure 1 Distribution of TB Patients Experiencing Side Effects of OAT in Intensive Treatment Stage (4 Weeks) at Cikampek Private Hospital




Source: Primary Data

The percentage description of the incidence of ADRs (Figure 1) above shows that the most common type of side effects of OAT experienced by patients with pulmonary TB during intensive treatment stage is red urine (100%), nausea (34.85%). Other effects that were experienced by many sufferers were shortness (27.27%) tingling (18.18%), dizziness (16.67%), no appetite (15.15%) and visual impairment (1.51%). The lowest effect was diarrhea (1.51%).

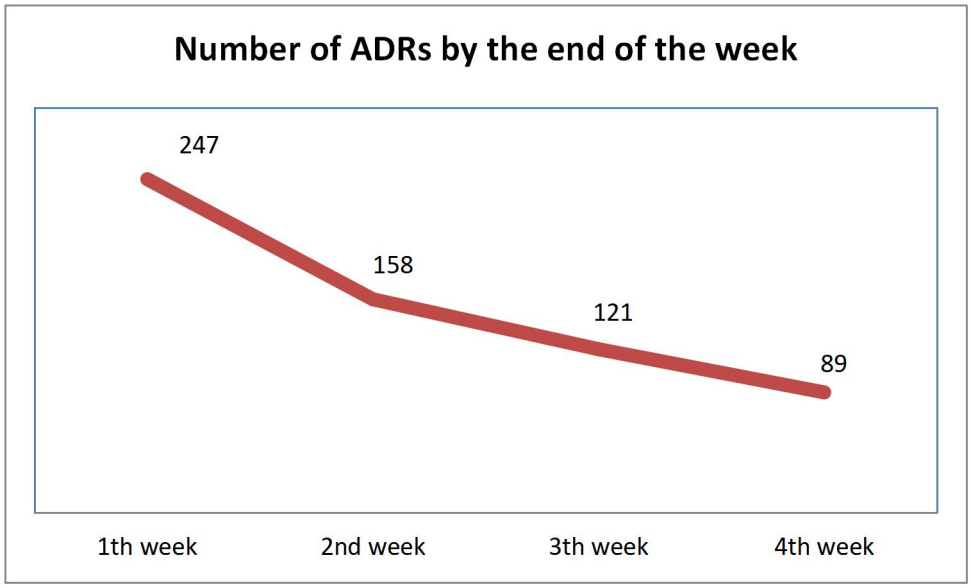



Figure 2. The total number of ADRs based on the results of interviews of all respondents at the end of the 1st, 2nd, 3rd and 4th week of new TB pulmonary TB patients at the Cikampek Private Hospital, April-September 2017.

Source: Primary Data

## IV. DISCUSSION

In contradiction various studies show that the ratio of sufferers based on gender (sex) can differ based on socio-demographic, socio-economic background, and time of study. Research conducted by Kusumawardhani (2015) at the West Java Sidawangi Paru Hospital in the January-June 2015 period showed that there were more female sexes. Of the total 126 patients, the majority of patients had a female sex of 71 patients (56%) and 55 patients (44%) male. Different things in evaluating the use of tuberculosis drugs in hospitalized patients in the Class III Treatment Room in One of the Houses Sick in Bandung by Sukandar, Hartini, Hasna. (2012) showed the number of men 54 (62.79%) more than 32 women (37.21%).

In a study at Cikampek Private Hospital more than half of respondents had a high school education background of 53 (63.86%) as the largest percentage of all respondents' educational levels. 2013 national data of pulmonary TB patients based on the characteristics of the level of education showed 0.4% did not finish school at most and tended to decline at a higher level of education. Some studies also report that socio-economic status is related to tuberculosis morbidity. Those who generally have lower secondary education become workers / employees with low economic status. Cikampek area is known as an industrial area that absorbs a lot of unskilled labor as factory employees.

Socio-demographic characteristics based on type of work as can be seen in table 1 above shows that laborers / employees with the largest percentage were 36 (43.37%) and were followed by entrepreneurs 29 (34.93%). Whereas for respondents who do not work 10 (0.12%), employees 5 (0.06%) and retirees 3 (0.04%). This is consistent with research led by Ogboi S. J. et al. (2010) at the primary health care center in Zaria, North-West Nigeria between May 2005-2006 which recorded 56.5% of clients with TB cases were employees. A study in South India by Gupta et al, (2011) reported that the majority of pulmonary TB patients were farm workers (25.2%) while the majority of extra pulmonary TB patients were housewives or entrepreneurs (18.92%).

The incidence of ADRs experienced by respondents included orange-red in urine, gastrointestinal syndrome, flu syndrome, peripheral neuropathy, respiration / shortness of breath syndrome. Generally, ADRs experienced by respondents began to be felt after seven days or after one week using OAT therapy, except red- orange in the urine begins to appear after the first day using OAT. The incidence of ADR in the form of urine that is red-orange is experienced by all 83 respondents (100%) included in this study. Generally, respondents claimed to have received an explanation from health workers who handled it about the orange-discolored urine when they first received OAT. It is as known that the red-orange discolo The handling of ADRs experienced by respondents with pharmacological interventions as shown in Figure 2 above has been proven to reduce the number of ADRs at the end of the 2nd, 3rd and 4th week. This is in accordance with research monitoring the side effects of anti-tuberculosis drugs (OAT) in the intensive treatment of pulmonary TB patients in Makassar City conducted by Abbas, A. (2017). The study showed that sufferers experience side effects of OAT every week during the intensive treatment phase. Side effects are more experienced in the first and second week and tend to decrease until the end of the intensive phase. The main type of side effect experienced by TB sufferers is joint pain.ration in urine as a result of side effects from the use of rifampicin.

Based on the results of the analysis using the traffic algorithm there are 91 (37.4%) ADRs with a score of 5-8 (probable ADRs) which indicate that the events that respondents felt were most likely due to ADRs from the antituberculosis drugs that respondents used. All respondents experienced the occurrence of ADRs in the form of red-orange urine with a definite degree of definite ADR. This means that the incidence of ADRs must be caused by the use of anti-tuberculosis drugs, namely rifampicin due to the metabolic process of drugs from rifampicin. The highest percentage of ADRs occurrence after red-colored urine with a certain degree of certainty ADR OAT primary is nausea, shortness of breath and itching.

## V. CONCLUSION

Based on research monitoring the side effects of antituberculosis drugs in patients with pulmonary TB in new cases at the Cikampek Private Hospital conducted in April-September 2017 some conclusions can be drawn as follows:

1. Socio-demographic description of the majority of Sundanese respondents with a percentage of female sex 39 (51.81%) and men 40 (48.19%) in the largest age group 18-35 years 40 (60.60%). The type of work most respondents 36 (43.37%) are laborers / employees with the highest educational background of 53 (63.86%).
2. Based on the results of the analysis using the Naranjo algorithm there were 91 (37.4%) ADRs with a score of 5-8 (probable ADRs) indicating that the event the respondents felt was most likely due to the ADR of the OAT that the respondents used.
3. Chi-square statistical analysis for each category with a p-value> 0.05 showed no relationship with the incidence of ADRs.

## VI. SUGGESTION

Suggestions from the results of this study are as follows:

1. The need to support tuberculosis control programs by designing appropriate strategies through education, promotion, communication, and monitoring tuberculosis mobilization programs in groups of people who are vulnerable to tuberculosis.
2. The role of pharmacists in managing the incidence of anti-tuberculosis drug ADRs, especially primary OAT to increase the success of therapy in TB patients.

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