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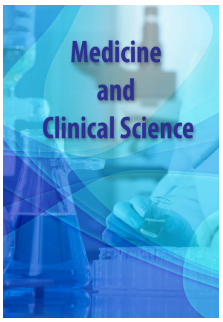

Factors Influence Side Effects and Withdrawal in TB patients resistant to Banten Province and West Java. In 2018-2020

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Abstract

Indonesia has committed to reducing the incidence of tuberculosis cases to 65 per 100,000 population by 2030. Efforts to control Tuberculosis in Indonesia in 2020-2024 are directed at accelerating Indonesia to achieve tuberculosis elimination by 2030, and ending the Tuberculosis epidemic in 2050, but 12-15% of TB treatment was not successful due to treatment drop out, drug side effects family support, motivation, drug taking supervisor to discontinue TB treatment. The aim of the study to know the factors that have the most role in drug side effects and resulting in the withdrawal of TB patients. The method was a retrospective cohort study, with a sample of 355 drug-resistant TB patients, percentage analysis, chi square analysis and multinomial logistic regression. Results showed withdrawal for total sample patients 33.2%, drop-out with side effect 20.8% and without side effect and withdrawal 12.4%. Withdrawal and side effect majority on female, lower education, income less than minimum wage regional, fat distance from health services. there was treatment monitor, was not support family, and there was health staff from health service. Correlation analysis of side effects, drug withdrawal and causative factors were gender, level of education, employment status, income, distance from home to health facilities, involvement of drug-taking supervisors, and support from health staffs. The final analysis that Side effect and drug withdrawal has a positive relationship only education level p 0.007, OR 2.311, 95%CI 1.257-4.251; while the protective factors were distance from home to health care facilities p 0.001, OR 0.334, 95%CI 0.178-0.626; healthcare support from health staffs p 0.001, OR 0.214, 95%CI 0.085-0.537; Confounding factors gender, employment status and family support. In conclusion, factors that influence the side effect and drug withdrawal were education, health services distance, health care support, and it was found that sex, working status, family support as confounding factors.

Background

The number of TB (Tuberculosis) cases that occur every year in the world was estimated at 10 million (range 9.0-11.1 million) people fall ill with TB in 2018. TB incidence was mostly in Southeast Asia (44%), Africa (24%) and Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8%), Americas (3%) and Europe (3%). Eight countries account for two-thirds of the global total: India (27%), China (9%), Indonesia (8%), Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa South Africa (3%) [1,2]. Drug Resistant Tuberculosis (RO TB) is still a threat in TB control and is a public health problem in many countries in the world [3,4]. Globally in 2019, it was estimated that 3.3% of new TB patients and 17.7% of previously treated TB patients were drug-resistant TB patients. In 2019, there were an estimated 9.96 million TB incidents worldwide, of which 465,000 were MDR TB/RR TB. Of the estimated 465,000 drug-resistant TB patients, only 206,030 were identified and 177,099 (86%) were treated, with a global treatment success rate of 57% [1,5,6].

In Indonesia, the estimation of drug-resistant TB is 2.4% of all new TB patients and 13% of patients who have been treated with a total estimated incidence of drug-resistant TB cases of 24,000 or 8.8/100,000 population [7]. In 2019, about 11,500 drug-resistant TB patients were identified and reported, about 48% of patients started second-line TB treatment, with a treatment success rate of 45% (WHO Global TB Report 2020) [1,8].

Based on West Java Health Profile data in 2017, tuberculosis cases in 2017 were reported as many as 82,063 cases, an increase of 13.16% compared to 2016 which was 72,558 cases [9]. Risk [6,7]. Tuberculosis in the three districts and cities ranged from 9-12% of the number of new cases in West Java. The incidence of Tuberculosis cases between men and women was more in men with a ratio of 1.3, while according to age group, the most cases were in the age group 15-24 years and the lowest is in the age group > 65 years. The decrease in TB

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case finding occurred in the age group 0-14 years, 25-34 years, while in other age groups there was an increase in the number of cases found.

In general, the number of tuberculosis case notifications per 100.00 population from 2003-2017 tends to increase, a significant increase occurred in 2017 which was 171 per 100,000 population compared to 2016 which was 149 per 100,000 population [10-12]. In 2017 there were three districts/cities with CNR all high Tuberculosis cases were in Sukabumi City (400), Cirebon City (396), Bandung City (386). The lowest CNR was Bekasi Regency (70). And for Drug Resistant TB cases from 2016-2019 there continued to be an increase in cases, namely in 2016 (490) cases, 2017 (1009 cases), 2018 (1566) cases and 2019 (2073) cases. Based on the Indramayu District Health Profile Data, the trend of TB case finding has increased over the last 3 years. Since 2016 the TB case finding has reached 2031 cases (43.9%). In 2017 TB cases reached 2722 cases (48.4%), in 2018 TB cases were 2578 cases (50.9%). and in 2019 there were 2601 TB cases (70%) with Drug Resistant Patients recorded and reported in 2016 as many as 12 cases, in 2017 there were 14 cases, in 2018 there were 31 cases, in 2019 there were 34 cases and in 2020 there were 32 cases. Meanwhile, patient drop out (DO) from year to year was still high (national target <5%). In 2018, the percentage of drug-resistant TB patients who dropped out of treatment was 25.80% and in 2019 it was 23.52% and in 2020 it was 23.33% [13].

In Banten Province, in 2016 drug-resistant TB became a public health problem and became a threat in TB control [12]. Based on data reported through the E-TB Manager, cases of drug-resistant TB in 2018 amounted to 138 people and in 2019 there were 225 people. Meanwhile, the dropout rate/loss to follow-up from year to year was still high above the target (national target <5%). In 2018, the percentage of drug-resistant TB patients who dropped out of treatment was 29% and in 2019 it was 11% [13].

Tuberculosis control efforts in Indonesia in 2020-2024 aim to: 1. Strengthen responsive management of Tuberculosis Control Programs starting from the center, provinces, districts, cities and health facilities. 2. Improving the quality of tuberculosis services that were centered on community needs 3. Increasing public access to Tuberculosis services 4. Increasing community needs and awareness of the importance of tuberculosis control [14]. The Tuberculosis control strategy in Indonesia 2020-2024 was implemented to achieve the target of reducing the incidence of Tuberculosis from 319 per 100,000 population in 2017 to 190 per 100,000 population and reducing the death rate from Tuberculosis from 42 per 100,000 population in 2017 to 37 per 100,000 population in 2024. However, the result, those patients were still found to be resistant due to discontinuation of treatment because one of them has side effects of TB medicine [15].

According to the Regulation of the Minister of Health Number 67, The following side effects may be caused by first-line ATM (Anti Tuberculosis Medicine): Isoniazid (H) bactericidal properties side effects are peripheral neuropathy (peripheral nerve disorders), toxic psychosis, impaired liver function, seizures; Rifampicin® bactericidal properties effect Flu (severe influenza symptoms), gastrointestinal disturbances, red urine, impaired liver function, thrombocytopenia, fever, skin rash, shortness of breath, hemolytic anemia; Pyrazinamide (Z) bactericidal properties effect gastrointestinal disorders, liver function disorders, gout arthritis; Streptomycin (S) bactericidal side effects were pain at the injection site, balance and hearing disorders, shock, anaphylaxis, anemia, agranulocytosis, thrombocytopenia; Ethambutol bactericidal properties effect visual impairment, color blindness, peripheral neuritis (peripheral nerve disorders) [16]. Meanwhile, according to the type of TB Drug Resistance, the Technical Instructions of the Ministry of Health in 2020, side effects that may occur include teratogenicity, heart problems, peripheral neuropathy, hearing loss, depression, hypothyroidism, sleep disorders, gastrointestinal disorders, liver function disorders, kidney function disorders, optic neuritis, arthralgia arthritis, skin discoloration, tendinopathy, tendon rupture, hematological disorders, lactic acidosis, convulsions, vestibular disorders [17]. In Banten Province, side effects has reported as follows dizziness, nausea, vomiting, skin discoloration, heart problems and arthritis, as well as in Indramayu Regency, West Java Province.

The meaning of this paper for TB public health

This means that after knowing the factors that have the most role in drug side effects and resulting in the dropout of TB patients, it is therefore important to convey it to Health Services in Banten Province and West Java Province, especially the Indramayu Health Office and related agencies to activate health workers to assist TB patients to comply with treatment and provide assistance when there are side effects on an ongoing basis and there is additional funds for monitoring TB cases that can be taken from the special operational assistance fund of the Minister of Health. In addition to direct visits, they are also monitored during treatment with digital monitoring of patients in TB treatment.

General objective

To find out the factors that cause side effects that affect drug withdrawal in patients with resistant TB in Banten and West Java Provinces. In the year of 2018-2020 and looking for a solution to the problem.

Specific objective

1. To know the distribution of the frequency of side effects, drug withdrawal, age, gender, education level, employment status, income, distance to health facilities, presence of medicine-taking supervisors, family support, support for health workers for drug-resistant TB patients in Banten Province and Regencies, West Java Province in 2021.
2. To know and prove the factors of age, gender, education level, employment status, income, distance to health facilities, presence of medication supervisors, family support, support from health workers to tackle side effects and drug withdrawal in drug-resistant TB patients in Banten Province and Regency, Indramayu, West Java Province in 2021.
3. To know and prove the most influential factors on side effects and drug withdrawal in drug-resistant TB patients in Banten Province and District, Indramayu, West Java Province in 2021.

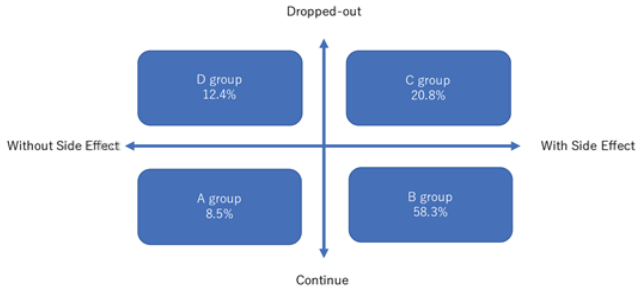
Research methods

Applied research, retrospective cohort design, population of all drug-resistant TB patients was 355 patients, in Banten Province 256 patients and Indramayu Regency 99 patients, West Java Province, 2018-2020. The analysis was descriptive of frequency distribution such as percentage, analysis with Chi Square, and multinomial logistic regression, used questioner

from national standard of TB treatment programmed in Indonesia, and have obtained research ethics.

Research result

Table 1 Sample size of 355 TB patients, distribution of the frequency of side effects, drug withdrawal, education level, gender, employment status, distance to health facilities, family support, support for health workers for TB patients with drug resistance in Banten Province and West Java Province in 2021.



Goup A without side effect and continue TB treatment amount 8.5%, with side effect and contnue TB Treatment 58.3%, with side effect and dropp-out treament 20.3%, ans wthout side effect and dropp-out TB patients 12.4%.

Based on the results of this study was important to serious attention for the patient the Long distance 11. 8%, there was no support from health workers 7.6% there are side effects and drug withdrawal is a target for the risk of death and TB transmission to other people, especially in the home, office and other environments who are in close contact with TB sufferers.

Side effects as follows: nauseous 102 (28,73%) patients, vomitus 30 (8.16%) patients, heavy vomiting 24 (6.76%) patients, dizzy 84(23.66%), weak 22 (6.20%) patients, shaky 2 (%) patients, can't wake up 7 (1.97%) patients, hearing disorders 3 (0.84%) patients, rest of them have not side effects 74 (20.85%). Dropout for long of treatment range 1 month until 4 months, and average 1.41 months. First Stage there were 7 types of TB medicine Bed aquiline, Levofloxacin, Clofazimine, INH, Pyrazinamide, Ethambutol, Ethionamide (4-6 months) have side effect as follows gastrointestinal disorder such as nausea, vomitus, dyspepsia, acute abdomen. Liver disfunction. Arthralgia, Arthritis. Advance stage of TB treatment there were 4 types medicine: Levofloxacin, Clofazimine, Pyrazinamide, Ethambutol. (5 months).

Bivariate analysis

Table 2. Analysis of Side Effects, Discontinuation of Drugs, Education Level, Gender, Employment Status, Distance to Health Facilities, Family Support, Support of Health Workers for Drug Resistance TB Patients in Banten Province and West Java Province in 2021.

Table 1. *Comparing the Characteristic and A.B.C.D Groups*

Characteristic	A group	B Group	C group	D group
Age				
≥35 years	20 (5.6%)	138 (38.9%)	37 (10.4%)	26 (7.3%)
20-35 years	10 (2.8%)	69 (19.4%)	37 (10.4%)	18 (5.1%)
Gender				
Male	21 (5.9%)	122 (34.4%)	36 (10.1%)	25 (7.0%)
Female	9 (2.5%)	85 (23.9%)	38 (10.7%)	19 (5.4%)
Education				
High	13 (3.7%)	124(34.9%)	31 (8.7%)	10 (2.8%)
Lower	17 (4.8%)	83 (23.4%)	43 (12.1%)	34 (9.6%)
Job				
Have Job	23 (6.5%0	117 (33.0%)	37(10.4%)	28 (8.0%)
No Job	7 (2.0%)	90 (25.4%)	37 (10.4%)	16 (4.5%)
Income				
≥minimum wage regional	14 (3.9%)	136 (38.3%)	28 (8.0%)	22 (6.2%)
<minimum wage regional	16 (4.5%)	71 (20.0)	46 (13.0%)	22 (6.2%)
Distance of Health Facility				
Close	19 (5.4%)	105 (29.6%)	32 (9.0%)	35 (10%)
Far	11(3.1%)	102 (28.7%)	42 (11.8%)	9 (2.5%)
Monitoring				
Yes	23 (6.5%0	155 (43.7%)	47 (13.2%)	35 (9.9%)
No	7 (2.0%)	52 (14.6%)	27 (7.6%)	9 (2.5%)
Family Support				
Yes	21 (5.9%)	162 (45.6%)	31 (8.7%)	7 (2.0%)
No	9 (2.5%0	45 (12.7%)	43 (12.1%)	37 (10.4%)
Medical Staff Support				
Yes	26 (7.3%)	171(48.2%)	47 (13.2%)	42 (11.8%)
No	4 (1.1%)	36 (10.1%)	27 (7. 6%)	2 (0.6%)

Table 2. *Side effects and drug withdrawal TB,*

No.	Variable	Side Effect		P	Relative Risk	95%CI RR	
		No	Yes	value		Lower	Upper
1	Age >35 Years No Drug withdraw Drug withdraws	 20(43.5%) 26 (56.5%)	 138 (78.9%) 37 (21.1%)	 0	 0.387 1.298	 0.194 1.060	 0.773 1.590
	20-35 Years No Drug Withdraw Drug Withdraws	10 (35.7%) 18 (64.3%)	69 (65.1%) 37 (34.9%)	0.005	0.307 1.487	0.185 1.194	0.508 1.845
2	Sex						
	Male No Drug withdraw Drug withdraws	 21(45.7%) 25 (54.3%)	 122 (77.2%) 36 (22.8%)	 0	 0.358 1.446	 0.218 1.160	 0.589 1.801
	Female No Drug withdraw Drug withdraws	 9 (32.1%) 19 (67.9%)	 85 (69.1%) 38 (30.9%)	 0	 0.287 1.356	 0.140 1.116	 0.591 1.648
3	Education						
	High No Drug withdraw Drug withdraws	 13 (56.5%) 10 (43.5%)	 124 (80.0%) 31 (20.0%)	 0.013	 0.389 1.197	 0.184 0.998	 0.821 1.436
	Low No Drug withdraw Drug withdraws	 17 (33.3%) 34 (66.7%)	 83 (65.9%) 43 (34.1%)	 0	 0.385 1.486	 0.233 1.196	 0.635 1.847
4	Working Status						
	working No Drug withdraw Drug withdraws	 23 (45.1%) 28 (54.9%)	 117 (76%) 37 (24%)	 0	 0.381 1.468	 0.239 1.174	 0.608 1.837
	No No Drug withdraw Drug withdraws	 7 (30.4%) 16 (69.6%)	 90 (70.9%) 37 (29.1%)	 0.045	 0.239 1.329	 0.105 1.104	 0.544 1.600
5	Income						
	≥ RMW No Drug withdraw Drug withdraws	 14 (38.9%) 22 (61 1%)	 136 (82.9%) 28 (17.1%)	 0	 0.212 1.619	 0.118 1.260	 0.382 2.081
	<RMW No Drug withdraws Drug withdraws	 16 (42.1%) 22 (57.9%)	 71 (60.7%) 46 (39.3%)	 0.045	 0,568 1,206	 0.325 0.995	 0.996 1.462
6	Distance from Home to Health Center						
	Near No Drug withdraws Drug withdraws	 19(35.2%) 35 (64.8%)	 105 (76.6%) 32 (23.4%)	 0	 0,293 1.773	 0.183 1,365	 0.471 2.303
	Far No Drug withdraws Drug withdraws	 11 (55%) 9 (45%)	 102 (70.8%) 42 (29.2%)	 0.152	 0.552 1.096	 0.244 0.952	 1.248 1.262
7	Drug Monitoring Services Availability						
	Yes No Drug withdraws Drug withdraws	 23 (39.7%) 35 (60.3%)	 155 (76.7%) 47 (23.3%)	 0	 0.303 1.519	 0.192 1.250	 0.478 1.847
	No No Drug withdraws Drug withdraws	 7 (43.8%) 9 (56.2%)	 52 (6.85%) 27 (34.2%)	 0.097	 0.475 1.175	 0.194 0.952	 1.163 1.451

8	Family Support						
	Yes No Drug withdraws Drug withdraws	21 (75%) 7 (25%)	162 (83.9%) 31 (16.1%)	0.241	0.623 1.085	0.285 0.925	1.360 1.273
	No No Drug withdraws Drug withdraws	9 (19.6%) 37 (80.4%)	45 (51.1%) 43 (48 9%)	0	0.36 1,550	0.190 1.225	0.684 1.962
9	Health Staff Support						
	Yes No Drug withdraws Drug withdraws	26 (38.2%) 42 (61.8%)	171 (78.4%) 47 (21.6%)	0	0.28 1.644	0.184 1,341	0.426 2.015
	No No Drug withdraw Drug withdraws	4 (66.7%) 2 (33.3%)	36 (57/1%) 27 (41.9%)	1	1.45 0.967	0.284 0.838	7.391 1.115

Based on Table 2. Side effects and drug withdrawal TB, age factor > 35 years who dropped out 37 cases (34.9%); age 20-35 years who dropped out of drugs 36 cases (22.8%); Gender male 36 cases (22.8%), female 38 (30.9%); Higher education 31 cases (20%), Low education 43 cases (34.1%); Working 37cases (24%), not working 37 (29.1%); income RMW 28 (17.1%), <RMW 46 cases (39.3%); Distance to health facilities near 32 cases (23.4%), long distance 42 cases (29.2%) ; There was no drugs Tb officer monitoring 47 (23.3%), no drug TB officer monitoring 27 (34.2%); Family support supports 31 (16.1%), does not support 43 (48.9%); Support from Health workers have supported 47cases (21.6%), have not support 27 cases (41 ,9%).

Correlation analysis of side effects and drug withdrawal of all factors were significantly related with $p < 0.05$, except for the presence and absence of side effects with drug withdrawal such as did not drop out of TB medicine and faraway of distance from health facilities p 0.152; no drug monitoring officer to medication of Tb patients p 0.097; family supports 0.241 and health workers do not support of Tb patients p 1.000.

Table 3. *Multivariate Analysis of Side Effects, Dropping Drugs, Education Level, Sex, Employment Status, Distance to Health Facilities, Family Support, Support of Health Workers for Drug Resistance TB Patients in Banten Province and West Java Province in 2021.*

No.	Variable	P value	RR	Lower	Upper	R Square (%)
1	Drug withdrawal	0.000	0,282	0.149	0.537	11.6
2	Education	0.007	2.311	1.256	4.251	14.6
3	Health Services Distance	0.001	0.334	0.178	0.626	17.1
4	Healthcare support	0.001	0.214	0.214	0.085	16.8
5	Sex	0.149	0.629	0.336	1.180	0.4
6	Working Status	0.100	0.588	0.312	1.106	2.1
7	Family Support	0.099	1.716	0.904	3,255	9.8 Total R2 29.2%

Multivariate analysis

According to Table 3, the final results of the multivariate analysis model showed that the factors that had a positive effect on the presence or absence of side effects of taking TB drugs with discontinuation and whether or not treatment turned out to be only the education factor, the distance factor for health facilities and the support of health workers had a negative effect RR <1 and $p<0.05$ which was a preventive factor, while gender, work status, and family support although the p value> 0.05 but cannot be excluded from the model because the RR changes more than 10%. The contribution of all variables to side effects and drug withdrawal was 29.2%, but when related alone, each variable has a significant effect >10%, such as the effect of distance from home to health facilities as much as 17.1%, support from health workers 16.8%, education level 14.6 % and 11.6% drop out of drugs, the rest such as gender, work status, and family support the effect was < 10%.

Discussion

EMany TB patients experienced side effects from taking TB drugs as many as 281 (79.2%), while 33.2% dropped out of drugs, TB patients had side effects and dropped out of drugs as many as 74 TB patients (20.84%). Patients who had side effects and dropped out of drugs for the most age were 20-35 years old 37 (34.9%); female gender 38 (30.9%); Low education 43 (34.1%); not working 37 (29.1%); income <UMR 46 (39.3%); Distance from house to health service facilities is far 42 (29.2%); no Drug Monitoring Services 27 (34.2%); The family did not support 43 (48.9%); Health workers do not support 27 (41.9%).

Side effects and discontinuation of all factors were significantly related with p < 0.05, except for side effects and whether or not there were side effects with discontinuation of drugs and not discontinuation of drugs at a distance from health facilities p 0.152; no supervisor taking medication p 0.097; family supports 0.241 and health workers do not support p 1.000. The final result of the multivariate analysis model found that the factors that had a positive effect on the presence or absence of side effects of taking TB drugs with discontinuation and whether or not treatment were found to be only factors of education, distance of health facilities and support of health workers had negative effects. RR < 1 and p < 0.05 which are preventive factors, while gender, work status, and family support even though the p value > 0.05 was not be excluded from the model because the RR changes more than 10%. The contribution of all variables to side effects and drug withdrawal is 29.2%, but if it is related alone, each variable has a significant effect >10%, such as the effect of distance from home to health facilities as much as 17.1%, support from health workers 16.8%, education level 14.6 % and discontinuation of drugs 11.6%. Gender, employment status, and family support influence < 10%. The side effects of patients receiving TB treatment were nausea, dizziness, hearing loss, blurred vision, vomiting and hallucinations, these occurred in both study sites. Eva Sartika Dasopong's research.[18] In 2020, the results of the study were 100% compliant with side effects that occurred itching, headache, nausea 72%, joint pain 45%, stomach pain 36.4%, no appetite and rash 27.3%, urine reddish color 18.2%. Putri Pamungkas' study of MDR TB patients was associated with no supervisor taking medication and side effects.[13] In this research nauseous 29,86%, vomitus 8.45%, heavy vomiting 6.76%, dizzy 24.51%, weak 6.20%, shaky 0.56%, can't wake up 1.97%, hearing disorders 0.84%. Majority of side effect this study compares with others study similar such as nausea. Joint paint, stomach pain and rash there was not any in this study. [20].

Age

This study revealed that the side effects and withdrawal are mostly found on the age 20-35 years (34.9% from population between 20-35 years old). This study was similar as Nevi and Titik Respati's study, which was significant in bivariate analysis but insignificant in multivariate analysis. The results of this study were different from the majority studies. Laíse Soares Oliveira Resende's[21,22] found that age >60 years group were the people who mostly dropped-out from TB Treatment due to the side effects. Laise Soares Oliveria samples are patients with HIV infection, anemia, alcoholism and liver disorders while in this study the patients were not HIV which rare consuming alcohol and experience liver dysfunction.[22]

Maria Klemens' research was related to drug withdrawal, while Eva Sartika Dasopang was a descriptive study in 2020 with the number of samples are 20 cases and 20 controls which found 11 TB patients aged 18-35 years (63.7% from the population). Sitti Farihatun's 2018 study in Jakarta patients dropped out of TB drugs by 44.6%, <1 month of treatment 61.2%, and taking more than 2 drugs and TB drug resistance 45.7%, the majority aged >64 years the proportion was 63.6%, infected with HIV 44.9%, very logical to drop out because of the elderly and heavy infected with HIV and TB. Other studies did not show the result of age factors.[18,23,24]

The main difference between this study and other studies was that it combines side effects and drug withdrawal with age, while other studies only drop out of drugs with the age factor. The concern was that the age of 20-35 years was a productive age, if this was not carried out seriously, it will become an active contagion in the community and harm the state.

Gender

It was found that 38 women (30.9% from female population) where drop-out the TB treatment, while the research, Nevi and Titik respati, [21] found that drug withdrawal in Sukamerang, Garut that the majority of those who dropped out of the treatment were men, Eva Sartika Dapong. the majority of whom were 54.5% men. Although different genders have an effect on drug withdrawal, bivariate analysis has the same effect on drug withdrawal, while multivariate was a confounding factor. Maria Klemens' study gender was not significantly correlation to drug withdrawal.[18,23] This study has the advantage of combining gender with side effects and drug withdrawal, while others studies only discuss drug withdrawal. Both male and female, with productive age, were found drug withdrawal and side effects that potentially becoming the source of transmission of TB [25].

Education

Education was a factor that affect drug withdrawal was found on the research of Irma Prasetyowati 6 (2) and Nevi & Titik Respati, while in this study education also affects drug withdrawal and the presence of side effects after taking TB drugs.[21,26] Maria Klemens' research found that Education was not related to drug withdrawal.

The advantages of this study also linked the side effects of TB drugs and dropouts to education which show a significant correlation. Low education is always a problem for drop-out treatment patients, because, mostly, they have lower income and less access to treatment due to the long distance. Consequently, they found several obstacles during the treatment, especially for those with weaken health condition. Therefore, the role of drug supervisors is important to give health education to the patient[23], facilitate assistances in taking medication on an ongoing basis to prevent drop out of the treatment and help overcoming the side effects of drugs. Educating TB patient and their family related compliance for completing the treatment, therapy, preventing and tackling side effects to avoid withdrawal TB treatment.

Work

This study shows that 37 (29.1%) not working experienced side effects and the end result of the working model was a confounding factor, Irma Prasetyowati's study was related to drug withdrawal, and Nevi & Titik Respati study was also associated with drug withdrawal, but this study Ari Budiman Himawan's work was not significantly related to this research. Other studies did not list work.[26,28] This study differs from other studies because it was related with side effects and withdrawal of treatment TB to work as confounding factors. Patients has not working with dropout of drugs was still in large numbers, especially with these side effects, it was very burdensome for the country and this endangers the community in their workplaces as transmitters of TB infection, the government, the private sector and the community need to be serious about controlling TB together in an integrated manner.[29]

Income

Side effects and drug withdrawal on income in this study were significant in bivariate analysis, but in multivariate

analysis income had no effect, Irma Prasetyowati's study of low income was associated with drug withdrawal, but multivariate analysis did not seem to have been carried out[26] The income of this study has no effect because the majority of patients who drop out of drugs have income <RMW equal to Irma's research deficit income, in 2015 in Situbondo the economic situation in Situbondo was very low at 5.75% below East and National Java [30] , while this study in Banten Province has a high economic growth of 8.95% and also Indramayu. This study combines side effects and withdrawal and income. Low income and dropouts as well as side effects are still quite high in Banten Province and Indramayu Regency, West Java Province, for free drugs from the government so as to relieve TB patients with low income, but a high burden on the state. Randy Adi Nugroho's qualitative research 8 informants paid for TB medication.[31] For low-income TB patients either working or not working due to low education, usually as laborers or farmers, they need to be given subsidies for transportation, nine basic commodities, money per month for other needs by the Government through the Ministry of Social Affairs, Ministry of Villages, Ministry of Home Affairs or CSR subsidies from the government and their place of work.[32,33]

Distance from Home to Health facilities

Irma's research the patients were used public transportation a lot, this study explains that access to health facilities was far related to side effects and drug withdrawal. Although they differ in explaining the distance factor, the meaning is the same in access to treatment with the location of health facilities and the distance from the patient's residence. The results of Irma Prasetyowati's research that public transportation was related to distance from health facilities[26], in this study the distance from health facilities to their homes was also significantly, except for the research of Maria Klemens, Nevi and Titik Respati Ari Budiman, Randy Adi Nugroho, distance was not significantly associated with dropout of TB drugs.[21,23,31,34] There are still many health facilities remotely from the homes of TB patients who take medication and experience side effects of 14.6%, the solution was long distance because this research is meaning full for health workers in overcoming drug withdrawal, it was better for health workers to periodically deliver drugs to long distance TB patients in Indonesia TB Control Programs have some funding to this activity such as Operational Health Assistance (BOK funding) from Ministry of Health, Global Fund, mutual cooperation from community etc. Monitoring TB treatment has already carried out from the Global Fund funding, and the Government has allocated the funding to hospitals to manage TB patients or other funds that allow for drug delivery to patients.[35,36]

Drug Monitoring Services by medication supervisor

The results of Irma Prasetyowati's research, Suci Kurnia's Research & Tri Krianto's, Drug Monitoring Supervisors were significantly associated with drug withdrawal in bivariate analysis, but multivariate analysis was not explained in these two studies.[26,37,38] In this study, drug taking supervisors in bivariate analysis also had the same significant results with side effects and discontinuation of TB drugs, but the multivariate analysis was not related because maybe the support of health workers to encourage taking medication was more involved and family support[39], Putri Pamungkas, MDR TB patients were associated with no supervisor. taking drugs and side effects Randy Nugroho qualitative research 8 (eight) informants did not have a drug-taking supervisor related to drug withdrawal.[40] Other studies did not include drug-taking supervisors related both of drug withdrawal and side effect, especially with side effects of TB treatment.[41–43]

Family support

Family support for drug withdrawal has a significant relationship in the research of Handayani, Suci Kurnia Sari and Tri Krianto, Pratama Adi Prabawa, Elysabeth Ria Widyastuti, Margareth Klemens not significantly associated with drug withdrawal.[37,44–47]. In this study, family who did not support TB treatment was identified as confounding factor to side effects and drug withdrawal. This means that family support is also needed for patient's compliance to medication as well as becoming an advisor and supporter during the treatment, especially when side effects occurred and continue to take medicine and seek efforts to overcome the side effects of TB drugs. Family has a big chance to support the TB patients [48]

Health Staff of Community Health Center Support

The support of health staff in the study was significantly related to side effects and drug withdrawal, while the research of Irma Prasetyowati, Suci Kurnia Sari & Tri Krianto, Nevi Nurkomaresari, Titik respati, Budiman, Laise Soares Olivera Resinde, Ayu Prameswari, Sari Handayani, Randy adi Nugroho, Tika Melani, Pratama Adiprabawa did not examine the factors of health worker support.[21,22,26,31,34,37,46,47,49,50]. The support of health staffs were very much needed for assistance, monitor and evaluation of treatment, health staffs from the Regional General Hospital, Banten Province and Indramayu District Hospital must be more active in monitoring their patients via telephone, WhatsApp, or could be visited directly if there is a problem. The funds were available at the hospital funds from the global fund, and other funds that possible to be used to visit TB patients, monitor treatment, adviser of side effect of TB treatment at the hospital.

Discussions for the success of overcoming the side effects of drugs that cause withdrawal in this study required the maximum role of health staff visitation to find out solution of drug side effects by providing assistance in the form of giving preferred foods and to overcome the side effects such as nausea, vomiting, dizziness, and weakness which mostly occur in patients. In addition, monitoring was also carried out with digital monitoring of TB patient treatment to prevent drop-out treatment. The Solution the distance between home and health facilities problem can be overcome by visitation from health staff. Expenses for direct visits can be allocated from the Special Operational Assistance (SOA) funding from the Ministry of Health and the Ministry of Finance, Village Funds, CSR, and others funding are also possible. This has been done successfully by Taskforce of COVID19 in Indonesia for tracing, testing and treatment activities to control Covid19.

Conclusion

In conclusion, factors that influence the side effect and drug withdrawal were education, health services distance, health care support, and it was found that sex, working status, family support as confounding factors..

Suggestion

Government and Communities are necessary to encourage serious treatment for monitoring and supervising the side effects of TB treatment to prevent drug withdrawal. Government that responsible for TB treatment such as the Indonesian Ministry of Health and Regional Government need

to work together with the Community, and motivate them to continue supporting their families suffering from TB. In addition, health staff are recommended to monitor TB patients actively and periodically for side effects observation of TB treatment, either direct visit or through communication media such as WhatsApp, direct telephone to TB patients. Moreover, the government could try to provide human resources from Health Students of Post Graduate/Bachelor or those who do not working to be given jobs that suitable with their interest to support TB patients completed their treatment.

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