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Association between the adequacy of preoperative antituberculosis treatment with abdominal postoperative morbidity and mortality on tuberculosis patients

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Introduction. The adequacy of tuberculosis treatment before abdominal surgery is a dilemma faced by surgeons who aims for low risk of morbidity and mortality. In addition, there is no data on morbidity and mortality post abdominal operation on TB patients in RSCM and RS Persahabatan. Therefore, this research aims to show the correlation between the adequacy of preoperative TB treatment and postoperative morbidity (fistula enterocutaneous, obstruction, and surgical site infection) and mortality.

Method. This study is a descriptive-analytic cross-sectional study done in Cipto Mangunkusumo Hospital dan Persahabatan Hospital using total sampling method, a total of 59 subjects with TB and had undergone abdominal operation and was admitted from January 2011 to August 2017, that fulfilled the criteria of this study. Bivariate and multivariate analysis using SPSS was done to analyze the correlation between TB treatment adequacy and postoperative morbidity and mortality.

Results 46 subjects (78%) did not receive adequate preoperative TB treatment. The morbidity rate in this study is 29 subjects 49.25% with significant correlation with the adequacy of preoperative TB treatment ($p = 0.030$). From the three morbidities in this study (fistula enterocutaneous, obstruction, surgical site infection), only surgical site infection (SSI) has significant correlation with TB treatment adequacy ($p = 0.048$). There is no significant correlation with postoperative mortality ($p = 0.564$). Compared to elective surgery, emergency surgery has higher morbidity (OR = 1.62; 95% CI 0.58 - 4.53) and SSI (OR = 2.02; 95% CI 0.63 - 6.46) incidence. A significant difference in the incidence of SSI between clean and dirty surgery wound was found ($p = 0.030$). Multivariate analysis showed that both adequacy of antituberculosis treatment and surgery type are independent risk factors for morbidity ($p = 0.025$).

Conclusion: Adequate preoperative TB treatment lowers the postoperative morbidity such as surgical site infection. There is no significant correlation between adequate preoperative TB treatment and mortality, and other morbidities such as fistula enterocutaneous and obstruction. Morbidity and SSI are more likely to happen in emergency surgery than elective surgery. Both adequacy of antituberculosis treatment and surgery type are independent risk factors for morbidity.

Keywords: Tuberculosis, treatment regiment, preoperative tuberculosis treatment

Introduction

Complications in patients with abdominal tuberculosis such as obstruction or perforation in a visceral organ such as the intestines need a surgical approach. Late management of these complications can cause mortality.¹

Abdominal tuberculosis and the adequacy of its treatment before abdominal surgery has caused surgeons to be faced with a dilemma whether the preoperative treatment is adequate to reduce the risk of morbidity such as enterocutaneous fistula and to reduce the risk of mortality. Antituberculosis drugs can reduce a substantial bacterial toxin, both local and systemic, reducing the symptoms, anastomosis leaks, and control abscess formation.² It recommended to administered preoperative antituberculosis drugs for two to four weeks to ensure the safety of the operation.² The American Society of Anaesthesiologist recommends that patients with active tuberculosis scheduled for an elective surgery need to be treated with preoperative antituberculosis drugs for two to three weeks until the patients are not infectious, clinically better, and negative sputum test found in three consecutive days to prevent the spread of *Mycobacteria tuberculosis*.³

To date, there is a lack of data regarding post abdominal surgery mortality and mortality in tuberculosis patients at dr. Cipto

Mangunkusumo and Persahabatan General Hospitals. Thus, a study aimed to find out the adequacy of preoperative oral tuberculosis drugs in association with post-surgical morbidity and mortality is required. Hopefully, the study may indicate the optimal time for abdominal surgery, and thus, post-operative morbidity and mortality may be reduced.

Method

This descriptive analytic study used cross sectional design, enrolling patients diagnosed with tuberculosis who underwent abdominal surgery by Digestive Consultant at dr. Cipto Mangunkusumo and Persahabatan General Hospitals from January 2011 to August 2017. Those with incomplete data on the medical records excluded from the study. Those immunocompromised (human immunodeficiency virus, routine corticosteroid therapy), diabetes mellitus, and malignancy also excluded. Subject's characteristics, nutritional status (using body mass index, BMI and subjective global assessment, SGA) including serum albumin level, type of surgery, wound degree, morbidities including surgical site infection (SSI), enterocutaneous fistula, and obstruction were the variables of independent. While the adequacy of antituberculosis treatment was a dependent variable. These

variables subjected to analysis using the Chi-square test or Fischer's exact test. Further analysis of risk factors using a multivariate logistic regression model.

The study approved by independent reviewer board of Faculty of Medicine, Universitas Indonesia. No961/UN2.F1/ETIK/2017.

Results

There were 59 subjects enrolled in the study, comprising of 38 (64.6%) males and 21 (35.6%) females. Subjects' ages ranged from 18–78 years old (mean 45.7 ± 18.9 years old), with 13 subjects (22%) of non-productive age (>65 years), and 46 subjects (78%) of productive age (18–65 years). Nutritional status in 27 subjects (45.8%) were underweight, 25 subjects (42.4%) were normoweight, and seven subjects (11.9%) were overweight. Serum albumin levels showed 45.8% subjects of <3 g/dL and 54.2% of >3g/dL. Types of surgery, which divided into emergency and elective surgery, showed as follows. Thirty-one subjects (52.5%) underwent emergency surgery and 28 subjects (47.5%) on elective surgery. The mortality was 5.1%, with 3 out of 59 subjects who died after surgery (emergency surgery consists of two subjects and elective one subject).

Table 1 Subject distribution

Distribution	Number	%
Duration of anti-tuberculosis treatment		
No antituberculosis	19	32.2
≤ 1 month	18	30.5
1 - 2 month	6	10.2
2 -< 6 months	3	5.1
≥ 6 months	13	22.0

Table 2 The frequency of morbidity

Distribution	Number	%
Morbidity		
Yes	29	49.25
No	30	50.8
SSI		
Yes	17	28.8
No	42	71.2
Obstruction		
Yes	6	10.2
No	53	89.8
Enterocutaneous fistula		
Yes	10	16.9
No	49	83.1

Table 3 Analysis of duration antituberculosis treatment

	No anti-antituberculosis	≤ 1 month	1–2 month	2-<6 months	≥ 6 months
Mortality					
– Yes	1	1	0	0	1
– No	18	17	6	3	12
Morbidity					
– Yes	10	11	3	1	4
– No	9	7	3	2	9
Enterocutaneous fistula					
– Yes	1	5	1	0	3
– No	18	15	5	3	10
SSI					
– Yes	6	6	2	1	2
– No	13	12	4	2	11
Obstruction					
– Yes	3	3	0	0	0
– No	16	15	6	3	13

Table 4 Surgery type analysis

	Laparoscopy	Non-laparoscopy
Mortality		
– Yes	0	3
– No	10	45
Morbidity		
– Yes	1	27
– No	9	21
Enterocutaneous fistula		
– Yes	0	9
– No	10	39
SSI		
– Yes	0	17
– No	10	31
Obstruction		
– Yes	1	5
– No	9	43

Table 5 Surgical wound degree analysis

	Clean	Clean-contaminated	Contaminated	Dirty
Mortality				
– Yes	0	1	2	0
– No	18	22	4	12
Morbidity				
– Yes	6	9	3	11
– No	12	14	3	1
Enterocutaneous fistula				
– Yes	1	4	1	4
– No	17	19	5	8
SSI				
– Yes	5	2	1	9
– No	13	21	5	3
Obstruction				
– Yes	0	3	1	2
– No	18	20	5	10

In the perspective of surgical wound degree classification, clean surgery found in 30.5% subjects, clean contaminated found in 39%, contaminated surgery found in 10.2%, and dirty/infected surgery found in 20.3%. of antituberculosis treatment and morbidity ($p = 0.030$). A significant association found between the adequacy of antituberculosis treatment with SSI ($p = 0.048$), but not with fistula ($p = 0.688$), obstruction ($p = 0.319$), and postoperative mortality ($p = 0.564$). We also found no significant association with the emergency and elective surgery groups ($p = 0.845$). However, we found the morbidity was 1.6x more likely to happen in emergency surgery compared to elective surgery (OR = 1.619; 95% CI 0.578 - 4.534). Similarly, there was also no significant difference between the incidence of SSI in emergency and elective surgery groups ($p = 1.417$), but SSI was 2x more likely to happen in emergency surgery compared to elective surgery (OR = 2.017; 95% CI 0.629 - 6.462). Furthermore, we found a significant correlation between dirty surgery wound and the incidence of SSI ($p = 0.030$), but no significant difference between SSI and clean-contaminated-, contaminated-, and dirty surgery of wound classification groups, respectively.

The multivariate analysis showed that both adequacy of antituberculosis treatment and surgery type were independent risk factors for morbidity ($p = 0.025$). However, neither adequacy of antituberculosis drug nor surgery type is an independent risk factor for SSI ($p = 0.069$).

Discussion

The mortality and morbidity of tuberculosis patients who underwent abdominal surgery remain a problem in our department of surgery. As shown in this study, those who receive inadequate preoperative antituberculosis treatment of up to 78%. However, we limited the study not to go further to

find out the underlying problems that lead a subject did not receive adequate preoperative treatment. The standard treatment depends on an infected organ, usually implies a 6-month regimen, which is sufficient for clinical tuberculosis. The first two months of the treatment focused on exterminating the rapidly replicating Mycobacteria. At this stage, clinical improvement may be noted. The next four months focused on eliminating the semi-dormant bacteria. At this stage, there will be a significant reduction in the colony of bacteria.

The morbidity in this study is 49.25%, and the bivariate analysis showed a significant association between the adequacy of antituberculosis treatment and postoperative morbidity. On the morbidities observed, SSI has a significant correlation with the adequacy of antituberculosis treatment. There is no significant association between adequacy of treatment with enterocutaneous fistula and obstruction. We also found a high incidence of SSI in subjects with inadequate antituberculosis treatment. SSI is the most complication found with the incidence of 28.8%. The incidence of SSI in adults at Digestive Surgery Division of Department of Surgery, CMGH, 2007, reported up to 10%. The study of Ke et al.,⁶ reported that the complications of non-thoracic surgery in subjects with pulmonary tuberculosis has higher postoperative complications rather than non-pulmonary tuberculosis. The complications reported are sepsis, pneumonia, stroke, acute kidney failure, myocardial infarct, pulmonary emboli, postoperative bleeding, and SSI.⁶ Although the subjects' characteristics were different from this study, subjects with adequate antituberculosis drugs may be considered as near-healthy subjects.

The high incidence of SSI as the complication identified in males, productive ages, and colorectal surgery. This finding paralleled to the report from Digestive Surgery, CMGH, of 56 cases SSI in 2012–2013, the majority found in males (60.7%). Males were more at risk of developing SSI and may have an association with the anatomical difference or the likelihood of skin colonization.⁷ The higher incidence of SSI in subjects of 25–65 years old aged might be related to the most surgery performed in those at a productive age.⁸ While the higher incidence of SSI in colorectal surgery following the findings of Wick et al. who found a higher risk of SSI in the contaminated and dirty surgery.⁹

Another predisposing factor of SSI is the nutritional status. The three indicators observed, namely BMI, subjective global assessment (SGA), and serum albumin level, showed that SSI found mostly in those with normal BMI, SGA category B, and albumin ≥ 3 g/dL. Another study of Satyanaranyaya et al. reported the incidence of SSI 48% in subjects with overweight or obesity, 45% in normal BMI, and 7% in malnourished subjects.³ SGA, as a measuring tool for nutritional status, is often used in adults and children. Some experts believed that serum albumin level correlates with immune function compared to other tools.¹⁰ Those with hypoalbuminemia experiencing dysfunction of cytokine metabolism, particularly interleukin-1 and defect of the complement system.¹¹ A study of Zheng et al. showed the correlation between hormones related to appetite, inflammatory cytokines, and BMI in

subjects with tuberculosis with or without diabetes mellitus. They concluded that abnormality in leptin and ghrelin correlated with low BMI during inflammatory response in tuberculosis with or without diabetes mellitus. Malnutrition is also a significant risk factor of the active onset of tuberculosis and poor prognosis.¹² Malnutrition affects the cell-mediated immunity which is the primary defence against tuberculosis.¹³

The higher incidence of SSI in emergency surgery correlated with insufficient preparation, underlying disease, and more often contaminated or dirty wound.¹¹ The postoperative mortality in this study shows no significant correlation with the inadequacy of antituberculosis treatment. According to Ke et al.,⁶ active pulmonary tuberculosis significantly correlates with 30-day postoperative mortality. Furthermore, the study of Ren et al.² found the correlation of adequacy preoperative antituberculosis treatment in spondylitis tuberculosis, i.e., recurrent and non-healing spondylitis tuberculosis. There are different recommendations regarding the standard administration. Firstly, those recommend 2–4 weeks and secondly those recommend for >8 weeks' administration preoperatively. In this study of Ren et al., there is no significant correlation between the recurrence or the incidence of non-healing spondylitis tuberculosis.

A reason why subjects with tuberculosis are prone to postoperative complications is pulmonary inflammatory response that may lead to sepsis. Besides, tuberculosis may develop extrapulmonary and superimposed by the opportunistic infection. Incomplete antituberculosis treatment may worsen the infection and vice versa. Thus, worsen the postoperative complications. In contrast, antituberculosis drugs showed adverse effects, particularly to liver and kidney, that may worsen the outcome. The study of Ke et al.⁶ showed higher mortality in subjects with antituberculosis treatment than those who are not.

On the bivariate analysis in the type of surgery and morbidity, we found no significant difference and SSI between the emergency and elective surgery groups. However, it shown that morbidity is 1.6 times more likely to happen in emergency surgery (OR = 1.619; 95% CI 0.578–4.534) and SSI are twice more likely to happen in emergency surgery compared to elective surgery (OR = 2.017; 95% CI 0.629–6.462). This finding is similar to the study by Oliveira et al.,¹⁴ who found no significant association between surgery type and SSI ($p = 0.10$). In contrast, a study of Cheng et al.¹⁵ showed a higher incidence of SSI in the emergency surgery group with a significant difference ($p = 0.000$). This study proposed that inadequate preoperative preparation of emergency surgeries may be responsible for such difference. Therefore, it concluded that the type of surgery affects the incidence of SSI when there is poor adherence to appropriate surgical techniques and preparation. The study also showed a significant association between the degree of the wound classification and the incidence of SSI, particularly between clean and dirty surgical wounds. Our findings differed from the study by Oliveira et al.,¹⁴ which reported no significant correlation. This showed that other factors must be evaluated alongside the surgical wound degree.¹⁴

Cheng et al.¹⁵ evaluated risk factors of SSI in teaching hospitals. The study concluded that the degree of the surgical wound was independently associated with SSI after multivariate analysis. The incidence of SSI on clean-contaminated, contaminated, and dirty differs significantly with a clean surgical wound degree. This study also showed a different result from Oliveria et al.,¹⁴ with our study. The different subjects' characteristics could explain this difference enrolled in this study. Our study involves population with comorbid tuberculosis which must receive tuberculosis treatment before surgery.^{14,15}

The difference in results could also be due to the difference in the classification of surgical wound degrees. Chan et al.,¹⁶ conducted a study on interrater reliability between surgeons, Swissnoso-trained infection clinical nurse (ICN), and histological findings in classifying surgical wound degrees in appendicitis. This study showed minimal match between the three but a moderate match between ICN and histological findings. Chan et al.¹⁶ suspected the possibility of that unreliability is because of the difference in understanding of the definition and the appropriate time to identify the surgical wound degree. Their study also showed that surgeons did not understand the classification. This issue may occur in this study, and thus further study can be conducted to ascertain this.¹⁷

In this study, secondary data were obtained from medical records. The medical record provides the duration of the tuberculosis treatment per subject, but the compliance could not be assessed.

Conclusion

The adequate antituberculosis drug in subjects with tuberculosis before abdominal surgery lowers the risk of postoperative morbidity. It significantly lowers the incidence of SSI. However, it does not show significant correlations with the incidence of enterocutaneous fistula, obstruction, and postoperative mortality. Morbidity and SSI are more likely to happen in emergency surgery than elective surgery, although not statistically significant. Multivariate analysis showed that both adequacy of antituberculosis treatment and surgery type are independent risk factors for morbidity.

Disclosure

The author(s) declare have no conflict of interest to disclose

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