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Impact of Underweight on the Unsuccessful Treatment Outcome Among Adults with Drug-Resistant Tuberculosis: A Systematic Review

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Abstract

Background: *The emergence of drug-resistant (DR) strains of Mycobacterium tuberculosis has disrupted the control of tuberculosis (TB) problem worldwide. Most of DR-TB patients present with underweight problems. Prior studies showed that body mass index affects sputum conversion and could be a predictor of treatment outcome, but the causal relationship has not been established yet. This systematic review aimed to determine the impact of underweight on the unsuccessful treatment outcome among adults with DR-TB.*

Methods: *Systematic literature search and handsearching were done in four databases: Cochrane, Proquest, Pubmed, and ScienceDirect. Filtering process by using selection criteria yielded 4 eligible articles (2 prospective cohort and 2 retrospective cohort studies) for answering the clinical question. Critical appraisal was conducted by using the Newcastle-Ottawa Quality Assessment Scale (NOS).*

Results: *All four studies were assessed as having high quality according to the NOS score. The findings of all eligible studies were consistent in revealing the impact of underweight on the unsuccessful treatment outcome in DR-TB, with the relative risk: 2.194 (95% confidence interval [CI]:=1.134–4.246), 1.771 (95% CI=1.069–2.931), 3.465 (95% CI=1.114–2.712), and 4.703 (95% CI=1.709–12.947), consecutively. The number needed to harm (NNH) of 3–7 indicated the clinically meaningful harm of the exposure. This systematic review showed that one poor outcome incidence could be found with only a few underweight DR-TB patients.*

Conclusion: *Underweight increased the risk of unsuccessful treatment outcome among adults with DR-TB. Low baseline body weight (<40 kg) could be another considerable factor in anticipating the poor treatment outcome.* ***(J Respirol Indones 2022; 42 (2): 161–9)***

Keywords: *drug resistant; tuberculosis; underweight; unsuccessful treatment outcome*

Dampak *Underweight* terhadap Luaran Buruk Pengobatan pada Pasien Dewasa dengan Tuberkulosis Resisten Obat: Telaah Sistematis

Abstrak

Latar belakang: *Kemunculan strain resisten obat (RO) dari Mycobacterium tuberculosis telah menghambat upaya pengedalian masalah tuberculosis (TB) di seluruh dunia. Underweight sering dijumpai pada pasien TB-RO. Studi-studi sebelumnya menunjukkan bahwa IMT dapat memengaruhi konversi sputum dan dapat sebagai prediktor luaran pengobatan, namun hubungan kausalnya belum ditetapkan hingga saat ini. Tinjauan sistematis ini bertujuan untuk menentukan dampak underweight terhadap luaran buruk pengobatan di antara pasien dewasa dengan TB-RO.*

Metode: *Penelusuran literatur tersistematis dan handsearching dikerjakan pada empat basis data: Cochrane, Proquest, Pubmed, dan ScienceDirect. Proses penyaringan dengan menggunakan kriteria seleksi menghasilkan 4 artikel yang memenuhi syarat (2 studi kohort prospektif dan 2 studi kohort retrospektif) untuk menjawab pertanyaan klinis. Telaah kritis dilakukan dengan menggunakan Newcastle-Ottawa Quality Assessment Scale (NOS).*

Hasil: *Keempat studi dinilai memiliki kualitas tinggi berdasarkan skor NOS. Temuan dari semua studi konsisten dalam memperlihatkan dampak underweight pada luaran buruk pengobatan TB-RO, dengan risiko relatif sebagai berikut: 2,194 (interval kepercayaan [IK] 95%=1,134—4,246), 1,771 (IK 95%=1,069—2,931), 3,465 (IK 95%=1,114—2,712), dan 4,703 (IK 95%=1,709—12,947), berturut-turut. Number needed to harm (NNH) sebesar 3—7 mengindikasikan bahaya yang signifikan secara klinis dari pajanan underweight karena hanya sedikit saja pasien dengan status underweight yang dibutuhkan untuk memperoleh satu insidens tambahan luaran buruk pengobatan TB-RO.*

Kesimpulan: *Underweight meningkatkan risiko luaran pengobatan yang tidak berhasil di antara pasien dewasa dengan TB-RO. Berat badan dasar yang rendah (<40 kg) dapat menjadi faktor lain yang perlu dipertimbangkan dalam mengantisipasi luaran buruk pengobatan.* ***(J Respirol Indones 2022; 42 (2): 161–9)***

Kata kunci: *luaran pengobatan buruk; resisten obat; tuberculosis; underweight*

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INTRODUCTION

Amidst the era of COVID-19 pandemics, tuberculosis (TB) remains an unsolved public health problem with high burden of morbidity and mortality. World Health Organization (WHO) reported that in 2019, 10 million (range, 8.9–11.0 million) people globally developed TB and this number has only been declining very slowly in recent years. In 2019, TB led to 1.4 million deaths worldwide, one of the top 10 causes of death overall and the leading cause of death from a single infectious agent. In 2020, predictably the global number of TB death increased by 0.2–0.4 million due to the sharp decrease in TB case notification between January – June 2020 in four contributing countries, i.e. India, Indonesia, Philippine, and South Africa (44%).[1]

Attempts to control TB threat become more challenging due to the emergence of drug-resistant (DR) strains of *Mycobacterium tuberculosis*, which is resistant to at least rifampicin and isoniazid.[2] In 2019, an estimated 500,000 (95% uncertainty interval, 400,000–535,000) people had rifampicin-resistant TB (RR-TB), of which 78% developed DR-TB.[1] Compared to the drug-susceptible ones, TB strains with drug-resistance are more difficult to treat.[3] According to the latest WHO report, only 57% patients with DR/RR-TB showed successful treatment outcome. The treatment for DR-TB demands longer time, more drugs, higher cost and more toxic.[1] Among the top 30 high DR-TB burden countries, Indonesia ranked fifth globally in 2018.[4]

The magnitude of problem in DR-TB treatment demands an understanding of factors that can interfere with the treatment response. Previous studies demonstrated that underweight is common among DR-TB patients prior to the initiation of treatment.[5,6] Several studies also reported the potential role of underweight in predicting the outcome of DR-TB treatment.[7–9] However, the causal relationship between underweight and the unsuccessful outcome of DR-TB treatment has not yet been established. Up until now, there has been no single systematic study in this field. Therefore, this systematic review aimed to determine the impact of underweight on the unsuccessful treatment outcome among adults with DR-TB.

METHODS

This systematic review was carried out based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement. The literature search was performed from February 6–8, 2021 in four databases: Cochrane, Proquest, Pubmed, and ScienceDirect; along with manual handsearching. Keywords of “multidrug resistant”, “tuberculosis”, “underweight”, and “unsuccessful treatment outcome” as well as their synonyms and related terms were used during the search. The keyword of “adult” was omitted due to the lack of results, but it did not necessarily impact the finding and study analysis. The terms applied in each of the databases are shown in Table 1.

Literature selection was conducted based upon inclusion criteria: (1) study on human; (2) comparative study; (3) observational study; and (4) journal/ research articles/ meta-analysis/ systematic reviews. The selection was done without any time or language restriction. The exclusion criteria were: (1) not relevant to the clinical question; (2) the reported results were not complete to be analysed in this systematic review; and (3) cross-sectional studies.

The data from each yielded study was extracted into a table, compiling study citations, baseline characteristics of subjects, operational definition of the determinant and the outcome, and the relevant finding. Study citations included the principal author’s name and year of publication. Baseline characteristics of subjects in each study involved the study location, number of subjects, age, and gender. The relevant finding comprised the odds ratio (OR)/hazard ratio (HR) from each study.

Table 1. Search Queries

Database	Terms	Articles Found	Articles Used
Cochrane	multidrug resistant OR multidrug-resistant OR MDR OR multi drug resistant OR multi-drug resistant OR drug-resistant OR drug-resistant in Title Abstract Keyword AND Tuberculosis OR Tuberculoses OR kochs disease OR koch s disease OR koch disease OR mycobacterium tuberculosis infection OR lung tuberculosis OR lung tuberculoses OR pulmonary tuberculosis OR pulmonary tuberculoses in Title Abstract Keyword AND underweight OR leanness OR thinness OR body weight OR body mass index OR BMI OR low body mass index OR low bmi in Title Abstract Keyword AND treatment failure OR failure to treat OR lost to follow up OR lost to follow-up OR death OR died OR mortality OR default OR unsuccessful treatment outcome OR poor treatment outcome in Title Abstract Keyword - (Word variations have been searched)	23	0
Proquest	ab(multidrug resistant OR multidrug-resistant OR MDR OR multi drug resistant OR multi-drug resistant OR Drug-Resistant OR Drug-Resistant) AND ab(Tuberculosis OR Tuberculoses OR kochs disease OR koch s disease OR koch disease OR mycobacterium tuberculosis infection OR lung tuberculosis OR lung tuberculoses OR pulmonary tuberculosis OR pulmonary tuberculoses) AND ab(underweight OR leanness OR thinness OR body weight OR body mass index OR BMI OR low body mass index OR low bmi) AND ab(treatment failure OR failure to treat OR lost to follow up OR lost to follow-up OR death OR died OR mortality OR default OR unsuccessful treatment outcome OR poor treatment outcome)	38	2
Pubmed	(((((((((multidrug resistant[Title/Abstract]) OR (Multidrug-Resistant[Title/Abstract])) OR ("MDR[Title/Abstract])) OR (multi drug resistant[Title/Abstract])) OR (multi-drug resistant[Title/Abstract])) OR (Drug-Resistant[Title/Abstract])) OR (Drug-Resistant[Title/Abstract])) AND ((((((((((Tuberculosis[Title/Abstract]) OR (Tuberculoses[Title/Abstract])) OR (Kochs Disease[Title/Abstract])) OR (koch's disease[Title/Abstract])) OR (koch disease[Title/Abstract])) OR (mycobacterium tuberculosis infection[Title/Abstract])) OR (lung tuberculosis[Title/Abstract])) OR (pulmonary tuberculosis[Title/Abstract])) OR (pulmonary tuberculoses[Title/Abstract])) OR (lung tuberculoses[Title/Abstract]))) AND (((((((((Underweight[Title/Abstract]) OR (Leanness[Title/Abstract])) OR (Thinness[Title/Abstract])) OR (body weight[Title/Abstract])) OR (body mass index[Title/Abstract])) OR (BMI[Title/Abstract])) OR (low body mass index[Title/Abstract])) OR (low bmi[Title/Abstract]))) AND ((((((((((treatment failure[Title/Abstract]) OR (failure to treat[Title/Abstract])) OR (lost to follow up[Title/Abstract])) OR (lost to follow-up[Title/Abstract])) OR (death[Title/Abstract])) OR (died[Title/Abstract])) OR (mortality[Title/Abstract])) OR (default[Title/Abstract])) OR (unsuccessful treatment outcome[Title/Abstract])) OR (poor treatment outcome[Title/Abstract]))	67	2
ScienceDirect	(Multidrug resistant OR multi drug resistant OR MDR) AND tuberculosis AND (underweight OR low body mass index OR BMI) AND (treatment failure OR unsuccessful treatment outcome)	4	0
Handsearching	multidrug resistant AND tuberculosis AND underweight AND unsuccessful treatment outcome	6	0

The quality assessment of the studies was performed by two reviewers independently. The eligible studies were critically appraised using the Newcastle-Ottawa Quality Assessment Scale (NOS) for cohort studies or the NOS for case-control studies. A minimum NOS score of 7 was required to define that the study was of high quality. Any discrepancy in the NOS score between reviewers were discussed to draw a conclusion. The flow of the study selection is summarized in the PRISMA flowchart, as shown in Figure 1.

RESULTS

The literature search yielded 51 studies that met the inclusion criteria and screening of duplication. From these studies, only ten articles passed the title and abstract screening.

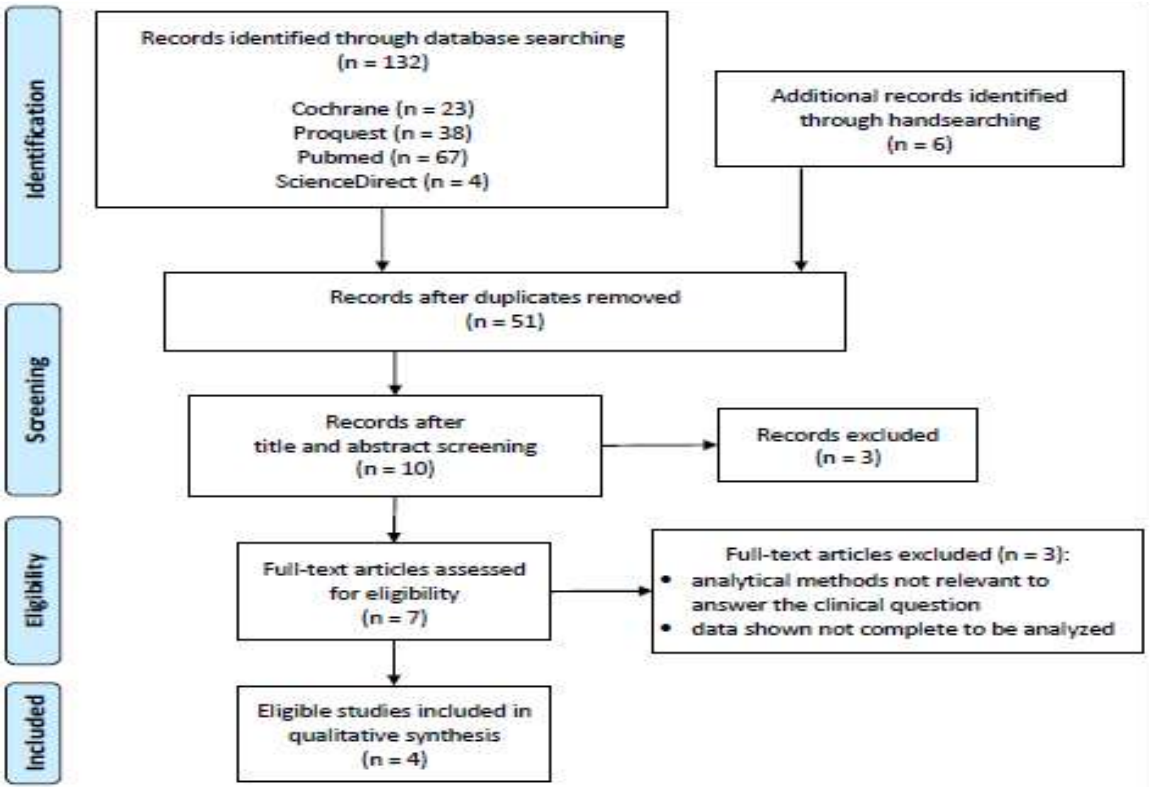

Figure 1. PRISMA flowchart of literature selection

Three of them were excluded due to irrelevant analytical method to answer the clinical questions or incomplete data. In the final analysis, there were four studies that met the eligibility criteria, i.e. Jaber et al[10], Ahmad et al[11], Khan et al[12], and Mitnick et al[13]

A summary of the baseline characteristics of each study is presented in Table 2. All eligible studies used cohort design and were categorized as level 2b based on the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence.

Jaber et al[10] conducted a prospective cohort study aiming to evaluate the risk factors associated with DR-TB and to explore the poor TB management in Yemen. They recruited 115 adult patients with DR-TB from the four major TB centers in Yemen, namely Al-Hudaydah, Taiz, Aden, and Sana'a. The enrollment was between January 1, 2014 and December 31, 2016. In this study, an overall success rate of 77.4% was reported. The relative risk (RR) of obtaining unsuccessful treatment outcomes among DR-TB patients with baseline body weight of ≤40 kg compared with those with baseline body weight of >40 kg was 2.194 (95% confidence interval [CI]=1.134–4.246) and the number needed to harm (NNH) was 5.088 (rounded up to 6). They confirmed that a baseline weight of ≤40 kg was associated with unsuccessful treatment outcomes among adult patients with DR-TB.

A prospective cohort study by Ahmad et al[11] aimed to evaluate management and predictors of unsuccessful treatment outcomes among DR-TB patients. This study was carried out at the Programmatic Management Unit for Drug-Resistant TB of Lady Reading Hospital, Peshawar, Pakistan, between 1 January 2012 and 28 February 2013. There were 196 DR-TB patients were consecutively enrolled for treatment and followed until January 31, 2015 or any outcome has been reported. In the final analysis, there were 181 DR-TB patients included since 15 others were excluded due to unknown treatment outcome. In this study, the overall treatment success rate was 75.1%. The RR of unsuccessful treatment outcomes among DR-TB patients with baseline body weight of <40 kg compared with those with baseline body weight of ≥40 kg was 1.771 (95% CI=1.069–2.931) and the NNH was 6.797 (rounded up to 7). This study suggested a higher risk of poor treatment outcomes in DR-TB patients with low baseline body weight.

Table 2. Characteristics and Relevant Outcome of the Yielded Studies

Article	Country	Study Design	Participants (mean/median age [years old]; male %)	Definition of Underweight	Definition of Unsuccessful Treatment Outcomes	Relevant Findings
Jaber et al[10]	Yemen	Prospective cohort (follow up time: at least 20 months after culture conversion, may be extended to 24 months for patients with extensive pulmonary damage)	115 subjects (NA; 56.5)	Baseline body weight of ≤40 kg	Treatment failure, died during treatment from any cause, lost to follow-up, or not evaluated	Multivariate analysis revealed that a baseline body weight of ≤40 kg was associated with unsuccessful treatment outcomes (AOR=25.09 [95% CI=1.80–34.9], *P*=0.016).
Ahmad et al[11]	Pakistan	Prospective cohort (follow up time: a minimum of 18 months after culture conversion, defined as two consecutive negative sputum cultures taken at least 30 days apart following initial positive culture)	181 subjects (31.5±14.7; NA)	Baseline body weight of <40 kg	Death, treatment failure and default	A higher risk of poor treatment outcomes was observed in patients with low baseline body weight (OR=2.966 [95% CI=1.186–7.419], *P*=0.02).
Khan et al[12]	Pakistan	Retrospective cohort (follow up time: at least 18 months after culture conversion, defined as two consecutive negative sputum cultures taken at least 30 days apart following initial positive culture)	186 subjects (37.07±16.34; 38.7)	Baseline body weight of ≤40 kg	Died, treatment failure or lost to follow up	In multivariate analysis, a baseline weight of >40 kg had statistically significant negative associations with the outcome of death and treatment failure (OR=0.256 [95% CI=0.109–0.602], *P*=0.002). The baseline body weight of ≤40 kg showed statistically significant association with lost to follow-up in univariate analysis (OR=9.816 [95% CI=1.256–76.728], *P*=0.029), but it did not reach the level of significance in multivariate analysis (OR=6.601 [95% CI=0.809– 53.868], *P*=0.078).
Mitnick et al[13]	Peru	Retrospective cohort (median follow up time: 40 months (range, 7 to 66) after therapy which lasted at least 18 months)	75 subjects (26.8 [11.8–65.1); 49)	Low BMI (the weight in kilograms divided by the square of the height in meters), defined as <18.5 for women and <20 for men	Treatment failure or death	Low BMI was found as a risk factor associated with the time to a poor outcome with adjusted HR of 3.23 (95% CI=0.90–11.53), *P*=0.004.

Note=*AOR*: adjusted odd ratio; *HR:* hazard ratio; *BMI*: body mass index; *NA:* not available/not known/not stated; *CI*: confidence interval; *OR*: odds ratio

Table 3. Quality assessment of studies based on Newcastle-Ottawa Quality Assessment Scale

Study	Selection	Comparability	Outcome	Total
Jaber et al[10]	****	**	***	9
Ahmad et al[11]	****	**	***	9
Khan et al[12]	****	**	***	9
Mitnick et al[13]	****	**	***	9

Table 4. Critical Appraisal of Cohort Studies

Characteristics	Jaber et al[10]	Ahmad et al[11]	Khan et al[12]	Mitnick et al[13]
Year	2019	2015	2019	2003
Study Design	Prospective cohort	Prospective cohort	Retrospective cohort	Retrospective cohort
Level of Evidence	2b	2b	2b	2b
RR (95% CI)	2.194 (1.134–4.246)	1.771 (1.069–2.931)	3.465 (1.114–2.712)	4.703 (1.709–12.947)
EER	0.361	0.338	0.550	0.438
CER	0.165	0.191	0.159	0.093
RRI	1.194	0.771	2.465	3.703
ARI	0.197	0.147	0.391	0.344
NNH	5.088	6.797	2.556	2.903

Note=*ARI*: absolute risk increase; *CER*: control event risk; *CI*: confidence interval: *EER*: experimental event risk; *NNH:* number needed to harm; *RR:* relative risk; *RRI*: relative risk increase.

A retrospective cohort study by Khan et al.[12] aimed to evaluate information regarding drug resistance pattern, detailed management, treatment outcomes and factors associated with unsuccessful outcomes in DR-TB patients at Baluchistan, Pakistan. They conducted this study at the Programmatic Management of Drug Resistant TB unit in Fatimah Jinnah General and Chest Hospital (FJGCH) Quetta, Baluchistan, Pakistan. In this study, 186 DR-TB patients receiving treatment at the study site from January 1, 2012 to April 30, 2016 were enrolled and followed until the treatment outcomes were reported. The overall treatment success rate in this study was 71.6%. This study found that the RR of unsuccessful treatment outcomes in patients with baseline body weight of ≤40 kg compared with those with baseline body weight of >40 kg was 3.465 (95% CI=1.114–2.712) and the NNH was 2.556 (rounded up to 3). They concluded that baseline weight of <40 kg emerged as a risk factor for unsuccessful outcomes in DR-TB patient.

Mitnick et al.[13] carried out a retrospective study with objective of identifying risk factors associated with poor outcomes and predictors of the time to death among DR-TB patients. They included 75 patients who enrolled in the community-based therapy for DR-TB in a poor section of Lima, Peru between August 1, 1996, and November 30, 1998. In this study, the overall treatment success rate was 76.0%. This study reported that the RR of poor treatment outcomes in patients with low BMI (<18.5 kg/m^2 for women and <20 kg/m^2 for men), compared to those with normal BMI, was 4.703 (95% CI=1.709–12.947) and the NNH was 2.903 (rounded up to 3). They drew a conclusion that low BMI was one of the predictors of the time to treatment failure or death in DR-TB patients.

All four studies were assessed as having high quality according to the NOS score. Details of the quality assessment of studies are shown in Table 3. Results of the critical appraisal of the studies are provided in Table 4.

DISCUSSION

Underweight has been thought to link with the poor outcome of DR-TB treatment. In this systematic review, four included studies with a total of 557 cumulative participants were consistent in highlighting the catastrophic impact of underweight on the outcome of DR-TB treatment, including death, treatment failure, default, and loss to follow up. From the four studies, we obtained the NNH ranging from 3 to 7, indicating that we only need to have 3 to 7 DR-TB patients with pretreatment underweight status to find a new incidence of unsuccessful treatment outcome. In line with our findings, study by Putri et al[14] with retrospective cohort study of 212 DR-TB patients in Persahabatan Hospital, Indonesia found that severely underweight patients (BMI of <16 kg/m^2), compared with normal weight or overweight (BMI ≥18 kg/m^2), was associated with longer time to initial sputum conversion (adjusted HR=0.55; 95% CI=0.37–0.84) and lower probability of sputum culture conversion within 4 months (adjusted RR=0.67; 95% CI=0.54–0.83).

However, a careful interpretation of studies should be made due to the use of different definition of unsuccessful treatment outcome among studies. Death and treatment failure were included as part of

observed outcomes in all studies, whereas lost to follow-up was only reported by Jaber et al[10] and Khan et al[12]. Ahmad et al[11] was the only study to report default as one of the poor treatment outcomes. Moreover, Khan et al[12] did not consider underweight as an independent risk factor for lost to follow-up because the statistical significance was not reached in the multivariate analysis. It was considered that the rate of lost to follow-up (7.5%) in study by Khan et al[12] was lower than the range reported by prior studies (18.3–27%).[15,16]

Another vigilant interpretation should also be applied regarding the use of baseline bodyweight, instead of BMI, in studies by Jaber et al[10], Ahmad et al[11], and Khan et al[12] to classify participants' nutritional status. As demonstrated by those studies, a cutoff baseline body weight of 40 kg could be suggested as a risk factor for unsuccessful outcomes in DR-TB patients. This cutoff value was based on the logistic regression model, with a fair discrimination power according to the receiver operating characteristic (ROC) curve analysis by non-parametric method (area under curve [AUC]=0.762; 95% CI=0.676–0.847, *P*<0.001).[12] No specific upper bound of age interval was mentioned by any study in their criteria of participant selection. This implied that the cutoff value of either BMI or baseline body weight could be applicable to all adults with DR-TB.

Possible mechanisms underlying the causal relationship between underweight and the unsuccessful outcome of DR-TB treatment have been provided by previous studies. Firstly, both innate and adaptive immune responses against *Mycobacterium tuberculosis* are blunted by undernutrition.[17,18] As demonstrated by a study of 56 individuals with latent TB, low BMI was significantly associated with decreased circulating levels of proinflammatory cytokines (IFN-γ, TNF-α, IL-22, IL-1α, IL-1β, IL-6), yet increased circulating levels of type 2 and regulatory cytokines (IL-10, TGF-β, IL-5, IL-13). It revealed that low BMI caused diminished protective cytokine response and increased risk of developing active TB.[19]

Secondly, underweight patients were more likely to present with more advanced disease. Podewils et al.[5] reported that DR-TB patients who were underweight, compared to normal or overweight, were at increased risk of having a higher culture colony count (≥3 colonies) with an OR of 2.7 (95% CI=1.6–4.5; *P*<0.001) and bilateral cavitation evident on chest X-ray with an OR of 2.8 (95% CI=1.8–4.3; *P*<0.001). Thirdly, underweight was believed to be linked with low serum drug levels. In undernourishment, the anti-TB medications are poorly absorbed through the gastrointestinal tract due to morphological changes and altered enzymatic activities.[20,21] Moreover, the renal clearance of unbound drugs also increases. All these factors subsequently result in sub-therapeutic serum levels of anti-TB drugs in underweight patients who are administered fewer dose of anti-TB medications according to their weight.[20] These may lead to high incidence of death and treatment failure among underweight patients with DR-TB.[12,20]

The limitations of this systematic review came up from the use of less accurate measure of the patients' nutritional status in three included studies, which used body weight instead of BMI in defining underweight since the participants' height was not measured. Hence, the BMI of the patients was unable to be calculated. Moreover, there was heterogenous use of the control group between studies. While one of the yielded studies limited the comparator group to only consisting of patients with normal BMI, other studies included patients with no upper bound of body-weight interval. The use of heterogeneous analytical variable made this systematic review could not be proceeded to a quantitative analysis (meta-analysis).

Therefore, we recommended future studies to use BMI as a standardized measure in classifying the nutritional status of patients, so the impact of underweight on the poor treatment outcome of DR-TB could be portrayed more clearly. Overall, this is the first systematic review to affirm underweight as the risk factor for the unsuccessful treatment outcome among adults with DR-TB. The results of this systematic review could be critical for the disease management as well as prevention.

This paper was presented at the 22nd International Meeting on Respiratory Care Indonesia (RESPINA) Virtual Conference, March 19—21, 2021 in Jakarta, Indonesia.

CONCLUSION

Among adults with DR-TB, underweight increased the risk of unsuccessful treatment outcome. Only in certain circumstances where the measurement of patients' height cannot be done simultaneously, low baseline body weight (<40 kg) could also be another factor to consider in anticipating the poor treatment outcome. Therefore, assessment of nutritional status (e.g., screening for malnutrition and identification of its causes) as well as nutritional care and support (e.g., nutrition counselling, dietary program, micronutrient supplementation as indicated) for DR-TB patients may play a pivotal role in improving the outcome of DR-TB treatment.

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