



Differences in Glutathione Peroxidase (GPx) Levels Before and After Pulmonary Tuberculosis Treatment

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DOI:

<https://doi.org/10.47134/phms.v3i1.557>

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Received: 03-11-2025

Accepted: 14-11-2025

Published: 29-11-2025



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Abstract: This study aimed to review changes in glutathione peroxidase or GPx levels or activity before and after pulmonary tuberculosis treatment. A systematic scoping review was conducted on articles published between 2016 and 2025 retrieved from Google Scholar, ScienceDirect, and PubMed. Article selection followed PRISMA guidelines and applied eligibility criteria based on the PICO framework. Six studies met the inclusion criteria and were included in the analysis. All reviewed studies reported changes in GPx levels or activity after tuberculosis treatment, with most showing an increase in GPx activity following anti-tuberculosis therapy. Several studies also reported that adjunct antioxidant interventions, such as N-acetylcysteine, contributed to enhanced glutathione system function and increased GPx activity compared to standard therapy alone. The observed increase in GPx activity was associated with reduced oxidative stress and improved redox balance during treatment. These findings indicate that GPx has potential as a biomarker for monitoring treatment response in pulmonary tuberculosis. However, variations in study design, sample size, and measurement methods were identified across the included studies. Further well-designed clinical studies with standardized GPx assessment protocols are needed to confirm its clinical utility and to clarify the role of antioxidant supplementation in supporting tuberculosis treatment outcomes.

Keywords: Glutathione Peroxidase, Oxidative Stress, Pulmonary Tuberculosis, Scoping Review

Introduction

Tuberculosis or TB has long been established as one of the infectious diseases that is still a global public health problem. The disease is caused by a bacterial infection of *Mycobacterium tuberculosis* whose transmission mainly occurs through the air. Once inhaled, the bacteria will reach the lower respiratory tract and settle in the lung tissue, making the lungs the most frequently affected organs (Choi et al., 2021). However, the spread of the bacteria to other organs such as lymph nodes, bones, kidneys, and the central nervous system can also occur, so extrapulmonary tuberculosis manifestations are still often found in clinical practice (Holmes et al., 2017; Organization, 2024).

Epidemiologically, tuberculosis still shows a high incidence rate in various parts of the world. Based on the latest global report from the World Health Organization, the number

of TB cases globally continues to increase from year to year. In 2023, the number of TB patients in the world is estimated to reach more than 10.8 million cases. This figure shows that the TB control efforts that have been carried out have not been fully able to reduce the rate of disease transmission (Banerjee et al., 2020). The Southeast Asian region is reported to be the region with the largest contribution of TB cases in the world, with a proportion of around 45 percent of the total global cases. The high burden of TB in this region indicates that there are structural and biological challenges that still need to be addressed comprehensively (Aggarwal et al., 2025; Behera et al., 2022; Santra et al., 2020).

Indonesia is included in the group of countries with the highest burden of TB in the world. Based on the latest Global Tuberculosis Report, Indonesia is reportedly ranked second after India in the number of TB cases. Every year, more than one million new cases of TB are found, with a relatively high mortality rate. This condition shows that TB is still a serious threat to public health in Indonesia and requires a more effective and sustainable control strategy (Ivanovich et al., 2017; Safe et al., 2021).

Various national programs have been designed and implemented to address TB, including increased case detection, standard therapy, and monitoring of treatment adherence. However, the achievement of success in TB treatment nationally is still reported to be below the set target. In 2023, the TB treatment success rate in Indonesia has not reached the global target of 90 percent. This shows that there are still challenges in the TB treatment process, both related to patient adherence factors, drug side effects, the emergence of drug resistance, and the body's biological response to the therapy given (Mahakalkar et al., 2017; Safe et al., 2021; Singh et al., 2020).

Evaluation of the success of TB treatment is a very important aspect in efforts to control this disease. So far, TB therapy evaluation has been carried out more through clinical examinations, sputum examinations, and radiological examinations. Although these methods have been widely used, limitations are still found, especially in assessing the body's biological response to therapy early and objectively. This condition encourages the need for additional approaches that can provide a more comprehensive picture of the healing process and response of TB therapy (Aggarwal et al., 2025; Leo et al., 2024).

In this context, the development of biomarkers for the monitoring and evaluation of TB treatment is getting more attention. The World Health Organization has set a target product profile as a strategic guide in the development of diagnostic, prognostic, and therapeutic monitoring tools for TB. Through this framework, the biomarkers developed are expected to be able to provide information that is fast, accurate, easy to apply, and suitable for use in health care facilities with limited resources. Biomarkers based on the pathophysiological mechanisms of disease are seen to have great potential in supporting the evaluation of TB therapy more effectively (Behera et al., 2022; Santra et al., 2020).

One of the pathophysiological mechanisms that are widely studied in tuberculosis is oxidative stress. Mycobacterium tuberculosis infection is known to trigger the activation of host immune cells accompanied by increased production of reactive oxygen species as part of the body's defense mechanisms. The production of these free radicals plays a role in killing bacteria, but if it occurs in excess, it can cause damage to lung tissue and worsen the

patient's clinical condition. An imbalance between free radical production and the capacity of the body's antioxidant system is known as oxidative stress and has been reported to contribute to the progression of TB disease.

To assess oxidative stress, various parameters have been used in biomedical research. These parameters include enzymatic and non-enzymatic antioxidants. Commonly reported enzymatic antioxidants include superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase. Meanwhile, non-enzymatic antioxidants such as reduced glutathione are also known to have an important role in maintaining the redox balance of cells. These parameters are considered to be able to provide an overview of the body's antioxidant status in the condition of infection and during the TB treatment process (Ighodaro & Akinloye, 2018; Leo et al., 2024; Ratnani et al., 2023).

Among these various antioxidant enzymes, glutathione peroxidase or GPx is seen as having a very important role. This enzyme functions to catalyze the reaction between reduced glutathione and peroxide compounds such as hydrogen peroxide and lipid peroxide which are toxic. Through these reactions, harmful compounds can be neutralized into molecules that are more stable and do not damage cells. During this process, the reduced glutathione will be oxidized into glutathione disulfide, which can then be reduced back by the body's antioxidant system.

The advantage of GPx over other antioxidant enzymes lies in the presence of a wide range of isoforms that are widely distributed across various tissues and cellular compartments. Unlike catalase which is mainly localized in peroxisomes, GPx is also found in the cytosol and mitochondria, so its ability to neutralize oxidative stress becomes more comprehensive. This wide distribution makes GPx a potential biomarker candidate for assessing systemic oxidative stress status in tuberculosis patients (Corr et al., 2020; Mengist et al., 2020; Tenny & Varacallo, 2025).

Although the role of GPx in the mechanism of oxidative stress has been widely reported, the results of studies regarding changes in GPx levels or activity before and after TB treatment still show variation. Some studies report an increase in GPx activity after TB therapy, while others suggest that the increase becomes more meaningful when accompanied by additional interventions such as antioxidant administration. This variation in results is influenced by differences in research design, subject characteristics, treatment phase, and examination methods used (Pizzino et al., 2020; Toossi et al., 2021; Venketaraman et al., 2020).

Therefore, an approach is needed that is able to collect and map the available scientific evidence in a systematic manner. The scoping review approach is considered appropriate to identify, evaluate, and synthesize various studies that address changes in GPx levels or activity in pulmonary TB patients before and after treatment. Through this approach, knowledge gaps can be identified and further research directions can be formulated in a more targeted manner (Kundu et al., 2022).

With this review, it is hoped that a more comprehensive understanding of the role of glutathione peroxidase as a biomarker for evaluation of pulmonary TB treatment can be

obtained. In addition, the results of this review are expected to serve as a scientific basis for the development of more effective TB therapy monitoring strategies and encourage further research on the role of various GPx isoforms during the treatment phases of pulmonary tuberculosis.

Methodology

This study was compiled using a non-experimental observational approach with a systematic scoping review design. This design was chosen to collect and map various scientific findings that discuss changes in levels or activity of the enzyme glutathione peroxidase before and after the treatment of pulmonary tuberculosis. The scoping review approach is used because the topic of study is still developing and the results of previous research are spread across various designs and research contexts.

The determination of the focus of the research was carried out through the identification of the role of the enzyme glutathione peroxidase as a biomarker of oxidative stress in pulmonary tuberculosis. To maintain clarity and consistency in the scope of the study, the Population, Intervention, Comparison, and Outcome frameworks are used as a conceptual basis. The population studied included patients with pulmonary tuberculosis, both active tuberculosis, latent tuberculosis, and drug-resistant tuberculosis. This study did not involve intervention or direct comparison. The outcome was a quantitative change in the level or activity of the enzyme glutathione peroxidase before and after treatment of pulmonary tuberculosis.

Literature search was carried out through several electronic databases relevant to the field of medicine and biomedicine, namely Google Scholar, ScienceDirect, and PubMed. The selection of such databases is based on the wide scope of publications as well as the availability of scientific articles relevant to the research topic. The search process was carried out using a combination of keywords related to pulmonary tuberculosis, glutathione peroxidase, and oxidative stress. The preparation of keywords is carried out by utilizing Medical Subject Headings and thesaurus to reach a variety of terms used in scientific publications. Boolean operators are used to combine keywords to make search results more targeted.

All articles obtained from the search results are collected and duplicate articles are deleted before the advanced selection process. The selection of articles is carried out in stages. The initial stage is carried out by examining the title and abstract to assess the suitability of the article with the focus of the research. Irrelevant articles are removed at this stage. Articles that pass the initial selection are then fully reviewed through a complete text check to ensure compliance with the inclusion and exclusion criteria that have been set.

The inclusion criteria in this study include articles that discuss the role of glutathione peroxidase enzyme in pulmonary tuberculosis patients, both in the context of pathogenesis, oxidative stress, and treatment evaluation. Articles with observational research designs such as cross-sectional, case-control, or cohort, as well as experimental studies are included in this study. In addition, the included articles must be available in full text, freely accessible, written in Indonesian or English, and published between 2016 and 2025. Articles excluded from studies when discussing only glutathione peroxidase unrelated to tuberculosis,

discussing other biomarkers without involving glutathione peroxidase, using non-human subjects, or discussing other diseases without comparison with tuberculosis.

The article selection process is documented using the PRISMA flow to describe the number of articles identified, screened, removed, to the final number of articles that meet the inclusion criteria. This documentation is carried out to ensure transparency and repeatability of the research process.

Articles that meet the inclusion criteria are then systematically extracted. The data collected included the title of the article, the name of the author and the year of publication, the design of the study, the objectives of the study, the characteristics of the subject, the method of measurement of glutathione peroxidase, the phase of treatment of tuberculosis studied, as well as the main results related to changes in glutathione peroxidase levels or activity. The extracted data is then compiled in the form of a synthesis table to facilitate analysis and comparison between studies (Ighodaro & Akinloye, 2018; Matuku-Kisaumbi, 2024; Singh et al., 2020).

Data analysis was carried out in a qualitative descriptive manner. The results of each study were not combined quantitatively due to differences in study design, measurement methods, and population characteristics. Synthesis is carried out by grouping research findings based on the direction of changes in glutathione peroxidase levels or activity before and after the treatment of pulmonary tuberculosis. Supporting factors such as treatment phase, use of antioxidant supplemental therapy, and comorbid conditions were also considered in the interpretation of the results.

The results of the analysis are presented in the form of a structured narrative description and supported by a synthesis table. The preparation of research reports follows the scientific structure of Introduction, Methods, Results, and Discussion to maintain consistency and readability. The completeness of reporting is evaluated using the PRISMA checklist to ensure that all important components of the scoping review have been presented systematically and can be scientifically accounted for.

Results and Discussion

Table 1. Synthesis Matrix

Synthesis Matrix						
Ye s	Author and year	Title	Research design	Purpose	Method	Main results
1	Sunil M. Mahakalkar, Dinesh Nagrale, Sanjay Gaur, Chetan Urade, et al. (2017)	Nacetylcysteine as an addon to Directly Observed Therapy Shortl therapy in fresh pulmonary tuberculosis patients:A randomized, placebocontrolle	Randomiz ed controlled clinical trial	To assess the effect of adjunct NAC administratio n in the intensive phase of DOTS-I (for 2 months) on several parameters.	The parameters studied included, examination of Acid Resistant Bacilli (BTA) in sputum, radiological improvement,	A total of 48 patients completed the study. The N-acetylcysteine (NAC) group showed better outcomes than placebo, with faster sputum conversion, more significant

Synthesis Matrix

Ye s	Author and year	Title	Research design	Purpose	Method	Main results
		d, doubleblinded study			levels of the enzyme Glutathione Peroxidase (GPx), body weight, and Mantoux response.	radiological improvement, and improved GPx levels and body weight at 2nd and 6th months. In addition, the immunological response was also better in the NAC group compared to placebo.
2	Izabella P. Safe, Eduardo P. Amaral, Mariana Araujo- Pereira, et al. (2021)	Adjunct N- Acetylcysteine Treatment in Hospitalized Patients With HIV-Associated Tuberculosis Dampens the Oxidative Stress in Peripheral Blood: Results From the RIPENACTB Study Trial	Randomiz ed clinical trial	The aim of this study was to find out whether supplemental therapy of N- acetylcysteine (NAC) in patients with tuberculosis (TB) and HIV co-infection who are undergoing anti-TB treatment can directly affect pro-oxidation and systemic inflammatory processes.	This study is a phase II prospective clinical trial assessing the effectiveness and safety of N- acetylcysteine (NAC) supplementat ion in standard therapy of pulmonary tuberculosis in patients with HIV in Brazil. Participants were divided into two groups: standard therapy (RIPE) and RIPE + NAC 600 mg twice daily for 8 weeks. Examinations include liver	The group of patients receiving N-acetylcysteine (NAC) showed significant improvements in glutathione (GSH) levels and total antioxidant status, as well as a significant decrease in lipid peroxidation compared to the control group. Changes in plasma cytokine levels occur only in small amounts. These results suggest that improvement of the body's antioxidant status through pharmacological interventions can be a rational strategy to reduce immunopathology associated with tuberculosis (TB)

Synthesis Matrix

Ye s	Author and year	Title	Research design	Purpose	Method	Main results
					function, antioxidant levels (GSH, SOD), oxidative stress markers (MDA, DNA oxidation), as well as cytokines and growth factors.	
3	Bazhora Yurii Ivanovic, Iermuraki Pavlo Petrovich, Pyatnitsky yurii S., et al. (2017)	Activity of the antioxidant system enzymes in patients with different clinical forms of the pulmonary tuberculosis	Case- control with pre- post evaluation	To evaluate the activity of antioxidant enzymes in different forms of pulmonary tuberculosis, by assessing their relationship to oxidative damage (carbonyl groups in plasma) before and after the intensive phase of treatment, as well as comparing the results with healthy individuals.	The study involved 83 tuberculosis patients aged 21–74 years at the Odessa Regional TB Clinical Hospital, with examinations conducted before and after 2 months of the intensive phase of standard therapy, as well as 23 healthy individuals as controls. The activity of the antioxidant system (AOS) is evaluated in peripheral blood. Samples are processed through 3000 rpm centrifugation	The activity of all enzymes studied in tuberculosis patients decreased significantly compared to the healthy control group. The most noticeable reductions occurred in SOD1, SOD2, GPx, and GR (more than 30% lower than controls). This decrease was accompanied by a significant increase in the level of protein carbonyl in plasma (up to 143% compared to controls). After two months of intensive therapy, there was a significant increase in antioxidant enzyme activity, but the value remained lower than in the control

Synthesis Matrix

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					to separate plasma and blood cells. The analysis included the activity of SOD1, SOD2, catalase (Cat), GSTP1, GPx, and GR enzymes in blood cells, as well as the levels of protein carbonyl in plasma. The protein concentration is determined by the Lowry method.	group. Similarly, protein carbonyl levels decreased after therapy, but did not reach normal values in healthy groups.
4	Ananyaashree Behera, Preeti Jain, Geetanjali Ganguli, Mainak Biswas, et al. (2022)	Mycobacterium tuberculosis Acetyltransferase Suppresses Oxidative Stress by Inducing Peroxisome Formation in Macrophages	In vitro molecular Experimental study	Identify the acetyltransferase enzyme Mtb encoded by the Rv3034c gene, which plays a role in the induction of peroxisome biogenesis as well as the oxidation pathway of β -fatty acids through interaction with macrophage receptors (MR). The researchers wanted to	Perform Mtb cell wall protein separation and identification through <i>ConA affinity purification</i> and <i>mass spectrometry</i> , as well as the conditional mutant generation of the Rv3034c gene using a suicide vector to evaluate the function of the gene. The analysis was	This study found that Mtb Rv3034c was able to suppress ROS production by inducing peroxisome biogenesis during the infection process. Peroxisomes contain various oxidase enzymes, such as catalase and glutathione peroxidase. The results showed that Rv3034c increased the expression of peroxisomal catalase, while the absence of Rv3034c decreased the

Synthesis Matrix

Ye s	Author and year	Title	Research design	Purpose	Method	Main results
				show that this enzyme has the potential to suppress the host's oxidative response	conducted to assess the expression of antioxidant enzymes such as catalase and glutathione peroxidase which play a role in overcoming oxidative stress. All experiments were conducted in Biosafety Level 3 laboratories in India, Germany, and the United States	expression of the catalase. This indicates that Rv3034c can detoxify oxidative radicals through an increase in the enzyme catalase. These findings support previous reports that Mtb has SOD and catalase enzymes to degrade ROS, thereby helping pathogens survive and replicate within macrophages.
5	Dr. Ankit Aggarwal, Dr. Poonam Singh, Dr. Kavita Dhar Bagati, Dr. Suruchi Mathur (2025)	A Study on role of Antioxidants in prevention of Hepatotoxicity induced by antitubercular drugs	Randomized controlled trial (RCT)	To study the level of oxidative stress markers in tuberculosis patients who experienced hepatotoxicity due to antituberculosis therapy (ATT). Also, to assess the role of the administration of exogenous antioxidants, namely vitamin E and	Patients who come to the pulmonary polyclinic at <i>Saraswathi Institute of Medical Sciences</i> are recruited and randomly allocated into three groups. One group consisted of patients who had recently been diagnosed with pulmonary tuberculosis	There was a statistically significant effect (p < 0.05) of drug interventions on the reduction of serum bilirubin, SGOT, SGPT, and ALP levels compared to the group without drug intervention. In addition, there was a statistically significant effect (p < 0.05) of drug interventions on increasing levels of antioxidant enzymes such as superoxide

Synthesis Matrix

Years	Author and year	Title	Research design	Purpose	Method	Main results
				vitamin C in combination, in tuberculosis patients who experience hepatotoxicity due to ATT therapy.	and had started antituberculosis therapy (ATT), while the other two groups consisted of patients who had experienced hepatotoxicity due to ATT. The fourth group consisted of normal healthy volunteers who were used as a control group.	dismutase (SOD), glutathione peroxidase (GPx), glutathione (GSH), catalase (CAT), and decreased levels of malondialdehyde (MDA).
6	Suman Santra, Debasree Bishnu, Gopal Krishna Dhali, Amal Santra, Abhijit Chowdhury (2020)	Expression of type I collagen in response to isoniazid exposure is indirect and facilitated by collateral induction of cytochrome P4502E1: An in-vitro study	In vitro molecular Experimental study	Determine the relationship between Isoniazid and CYP2E1 activation, See if increased CYP2E1 activity due to Isoniazid exposure can lead to oxidative stress and activation of liver stellata cells (HSCs), Prove that increased production of	This study used human liver stellata cells LX2 to examine the effects of isoniazid (INH) on oxidative stress and liver cell activation. Cells were cultured in a DMEM medium and given 5 µM INH for 24–72 hours, with or without antioxidants (N-acetyl-L-	This in vitro study showed that exposure to isoniazid (INH) in liver stellata cells (LX2) led to increased oxidative stress through activation of CYP2E1 and NOX2 enzymes, which triggered the production of Reactive Oxygen Species (ROS) and lipid peroxidation. Increased ROS is accompanied by decreased glutathione (GSH) levels as well as increased

Synthesis Matrix

Ye s	Author and year	Title	Research design	Purpose	Method	Main results
				type I collagen (which plays a role in liver fibrosis) is not a direct result of Isoniazid, but rather an indirect result through oxidative mechanisms mediated by CYP2E1.	and inhibitors (DPI, CMZ). Tests were carried out for antioxidant enzyme activity, lipid peroxidation, CYP2E1 and NOX activity, and ROS production. Gene/protein expression (α -SMA, collagen I, TGF- β , MMP, TIMP-1) was analyzed by qRT-PCR and western blot, while cell proliferation was assessed by MTT assay. Data analysis using the Student's t-test ($p < 0.05$	glutathione peroxidase (GPx) activity in response to oxidative stress. (102.63 ± 3.36 U/mg protein/min) compared to controls (64.64 ± 1.53 U/mg protein/min) Treatment with antioxidants such as N-acetylcysteine (NAC) and Tempol was shown to reduce ROS formation. These findings suggest that INHs can trigger oxidative stress and potentially cause hepatotoxicity through the CYP2E1-NOX2-ROS pathway.

Based on the six journals analyzed, the presence of changes in glutathione peroxidase levels or activity before and after pulmonary tuberculosis treatment has been consistently reported. In the study of Mahakalkar et al. (2017), an increase in serum GPx levels was reported after the addition of N-acetylcysteine (NAC) to antituberculosis drug therapy. In the study, blood GPx levels were measured in 48 subjects divided into two groups using Semi-Auto Analyzer in the 2nd and 6th months of treatment. The increase in GPx levels that occurred was accompanied by improvements in the radiological picture and an increase in the patient's weight. These findings are reinforced by the results of sputum conversion to negative that are reported to occur more quickly, so that the increase in GPx facilitated by NAC is considered to play a role in suppressing the production of reactive oxygen species and decreasing excessive TNF- α expression. Before the study was conducted, NAC was known to be able to increase reduced glutathione levels, decrease lipid peroxidation, and

reduce ROS levels. The addition of NAC in TB treatment was also discussed by Amaral et al. (2021) in TB patients with HIV comorbidities. Although GPx levels are not measured directly, NAC is described as a glutathione precursor related to GPx-4's activity as an antioxidant. In the study, an increase in total antioxidant capacity and glutathione levels was observed in standard TB therapy, but a more significant improvement was reported after the addition of NAC, so that improvement in the function of glutathione-based antioxidant systems may be indicated indirectly.

In the study of Ivanovich et al. (2017), antioxidant enzyme activity in patients with infiltrative pulmonary TB and pulmonary tuberculosis was evaluated before and after treatment. Increased activity of antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase, was reported after two months of TB treatment, especially in the infiltrative TB group. These findings suggest that the imbalance between oxidative stress and the antioxidant system can be corrected through TB therapy. In addition, the association between GPx levels and the rate of oxidative damage in patients with more severe disease degrees was reported to be attenuated or almost disappeared after treatment. This condition is in line with the mechanism of action of GPx in pulmonary tuberculosis, where in the early phase of the disease there is a disturbance of the redox balance which is greatly influenced by the function of first-line antioxidants. Although the body's antioxidant defense system reportedly improves and oxidative damage decreases after therapy, full recovery has not been achieved because the changes that occur are affected by complex interactions between drugs, endogenous antioxidant systems, as well as medication side effects. Based on these findings, severe disruption of the antioxidant system in TB patients was declared, so monitoring of antioxidant parameters such as AOS and carbonyl groups was considered useful to evaluate the success of treatment. Therefore, enrichment of standard TB therapy with additional interventions focused on restoring antioxidant balance is recommended (Leblanc et al., 2023; Meng et al., 2022; Page et al., 2021).

In addition, the role of peroxisome organelles in modulating oxidative stress during *Mycobacterium tuberculosis* infection was highlighted in the study (Behera et al., 2022) In the study, peroxisome biogenesis was reportedly induced by the Mtb protein encoded by the Rv3034c gene during the infection process. The peroxisomes that form reportedly contain a variety of antioxidant enzymes, including catalase and glutathione peroxidase, which play a role in modulating the host cell's redox environment and helping bacteria deal with the host's immune response.

Tuberculosis first-line drugs such as isoniazid and rifampicin are known to have hepatotoxic potential through mitochondrial permeability transition mechanisms and mitochondrial oxidative stress in liver cells, so additional protection is considered necessary. In research (Aggarwal et al., 2025) Increased mitochondrial glutathione levels were reported after methionine administration, which was found to help prevent more severe liver damage. The formation of free radicals such as superoxide anion and hydrogen peroxide is known to increase during TB treatment, both in the mitochondria and through

the activity of the cytochrome P450 enzyme in the liver. In these conditions, the role of GPx is crucial because this enzyme is in charge of neutralizing hydrogen peroxide and lipid peroxide into water through the use of reduced glutathione which is then converted into oxidized glutathione. Although oxidative stress is generally reported to decrease after TB treatment, recent research suggests that hepatotoxic side effects may actually exacerbate oxidative stress, which is characterized by a sharp decrease in superoxide dismutase levels in the group without antioxidant intervention. Therefore, the addition of antioxidants is considered necessary to increase the effectiveness of TB treatment. Increased GPx and catalase levels were reported to be better in the intervention group than in the non-intervention group, although GPx levels in patients receiving TB therapy remained higher than in the untreated condition.

Similar findings were also reported by Santra et al. (2020) in an in vitro study that evaluated isoniazid exposure to liver stellata cells. Activation of the CYP2E1 enzyme and increased oxidative stress were reported after isoniazid treatment for 72 hours. The condition was followed by a significant increase in GPx activity in liver stellata cells, suggesting a cellular compensatory response to compensate for the increase in ROS and the decrease in glutathione levels induced by isoniazid.

Conclusion

Based on the results of a review of six journals analyzed, changes in glutathione peroxidase levels or activity before and after treatment of pulmonary tuberculosis have been consistently reported. After the administration of tuberculosis therapy, the tendency to increase GPx activity was found in various study designs, both in pulmonary tuberculosis patients without comorbidities and with comorbidities. The increase in GPx activity showed an improvement in the body's antioxidant defense system along with a decrease in oxidative stress during the treatment process.

The addition of antioxidants such as N-acetylcysteine is reported to be able to strengthen the increase in GPx activity and glutathione system, resulting in a better clinical response to tuberculosis treatment. The improvement was shown through a decrease in oxidative damage, an increase in antioxidant capacity, and improvements in clinical and laboratory parameters. Nevertheless, the recovery of the antioxidant system has not been fully optimal due to the complex influence between drug effects, oxidative stress, and cellular compensation mechanisms.

Overall, glutathione peroxidase has potential as a biomarker for monitoring the success of pulmonary tuberculosis treatment. These findings support the need for further research with a stronger clinical design to assess changes in the activity of various GPx isoforms during the treatment phase of tuberculosis, as well as to evaluate the role of antioxidant interventions as adjuvant therapies in improving treatment effectiveness.

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