Abstract: Introduction: M. tuberculosis pyrazinamidase (encoded by the pncA gene) is a metalloprotein that in its metal binding site was found to hold a Fe\(^{2+}\) ion coordinated by one aspartate (Asp49) and three histidines (His51, His57, His71). Pyrazinamidase (PncA) activates the first-line antituberculous drug pyrazinamide into pyrazinoic acid. Emergence of strains resistant to PZA linked to mutations in the pncA gene. The concomitant mutations can decrease hydrolytic activity by structure changing that can effect on metal binding site. In order to first we detected how mutations effect on mutant pyrazinamidases activity in absence and > metal ions.

Methods: Wild type and mutant PZAses were cloned and expressed. Their activities were assayed by a qualitative colorimetric method according to Wayne test and presence of a red color detected by visual inspection. Then enzyme activities were determined in Mg\(^{2+}\), Ni\(^{2+}\) ions, at a final concentration of 1 and 2 mM. Our assay results indicated that 1 of 3 recombinant PZAses of PZA-resistant M. tuberculosis clinical isolates (containing T160P) had almost no activity, whereas other PZAses of PZA resistant isolates displayed less activity. Also the results obtained from this study indicated enzymatic activity of recombinant PZAses can be increased by Ni \(\text{Fe}^{2+}\) ions while in the presence of other metals activity of different recombinant PZAses indicated no or less changing.

Conclusion: These results suggest that mutations in recombinant PZAses altered the enzymatic activity according to the localization of the mutation and the type of substitution and also some metals can increase mutant pyrazinamidases activity by more effective interactions.

| M. tuberculosis, Pyrazinamidase, Pyrazynamide, Mutation, Resistance | Presentation: Poster |