Review Article

Causality assessment of adverse drug reactions: A machine learning approach

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ABSTRACT

Introduction: *Tuberculosis, caused by Mycobacterium tuberculosis, has a reported incidence of 2.77 per 1 lakh population in 2022 with a mortality of 0.32 per million. Acquired Immunodeficency Syndrome is caused by Human Immunodeficiency virus (HIV) which is characterised by marked immune suppression resulting in opportunistic infections. There are various adverse drug reactions reported with the anti-tubercular and anti-retroviral therapy. The present study attempts for causality categorization by machine learning algorithm.*

Materials and methods: *The present study comprises of 60 cases of adverse drug reaction in patient on either anti-tubercular or anti-retroviral therapy. To predict the causality category, a neural network was designed with a single input layer, two middle layer and a output layer. The train model was assessed on test cases to find accuracy of prediction of causality category.*

Results: *Mean age of cases was 35.92 ± 16.9 yrs. Mean weight of the cases were 50.36 ± 12.8 kgs. The underlying disease were pulmonary tuberculosis 71.7%, MDR tuberculosis 11.7%, extra pulmonary tuberculosis 8.3% and PLHA 8.3%. Out of 60 cases of adverse drug reactions, 2 cases were hospitalised and 1 case died. Various adverse reactions noted were hepatitis (18.33%), peripheral neuropathy (16.67%), rashes (11.67%), vomiting (11.67%), itching (8.3%). Other rare reactions included visual disturbances, psychosis etc. Out of 60 cases,54 cases were of possible causality category and 6 cases were of probable category. The overall accuracy of trained neural network on test cases was 62.5%*

Conclusion: *Causality assessment can be done by machine learning algorithm, which may help in pharmacovigilance practices.*

INTRODUCTION

Tuberculosis (TB) and Acquired Immunodeficiency Syndrome (AIDS) continue to persist as significant challenges, demanding increased attention due to their profound impact on communities worldwide. The causative agent responsible for Tuberculosis, namely Mycobacterium tuberculosis[1] exhibited an incidence rate of 2.77 in the year 2022, accompanied by a mortality rate of 0.32 per million individuals. These statistics underscore the persistent threat posed by TB and highlight the urgent need for robust management strategies.

Concurrently, Acquired Immunodeficiency Syndrome, which is caused by the Human Immunodeficiency Virus (HIV), represents a condition characterized by severe immune suppression, rendering individuals highly susceptible to opportunistic infections[2]. Notably, India has observed a declining trend in the HIV epidemic, with the prevalence dropping from 0.56% in 2000 to 0.20% in 2022. This positive trend is mirrored by a parallel decrease in AIDS-related deaths, with the number decreasing from 14.34 in 2010 to 2.90 per 1 lakh population[3] in 2022.

Despite these encouraging statistics, the effect of HIV on the immune system introduces complexities in the management of coexisting conditions, necessitating a nuanced understanding of potential complications, particularly unfavourable drug reactions.

The foundation of managing Tuberculosis and HIV lies in the provision of essential treatments, such as anti-tubercular and anti-retroviral therapies, respectively. However, the successful administration of these therapeutic regimens encounters challenges evident in the multitude of unfavourable drug reactions that have been documented in clinical practice. These adverse reactions not only impact the well-being of patients but also pose significant obstacles to treatment adherence and overall health outcomes[4].

Given this context, the present study embarks on a critical investigation into the domain of unfavourable drug reactions associated with anti-tubercular and/or anti-retroviral therapies. Recognizing the complexity of assessing causality in these situations, the study adopts a cutting-edge approach, employing

machine learning algorithms to classify the causality of these reactions. By integrating technology into the evaluation process, this research aims to provide a systematic and advanced framework for comprehending and categorizing unfavourable drug reactions. This contribution seeks to drive the ongoing development of precision medicine in the realm of infectious diseases, with the ultimate objective of refining healthcare practices and improving patient outcomes.[5]

MATERIALS AND METHODS

In this investigation, a total of 60 cases of unfavourable drug responses[1] in patients receiving either anti-tubercular or anti-retroviral treatment were examined. In order to establish the causality classification of these responses, a neural network was constructed, comprising a solitary input layer, two intermediary layers, and an output layer. The neural network was trained using the accessible data, and its capacity to accurately assign causality classifications was assessed using a collection of test instances. The objective of this methodology was to evaluate the dependability of the neural network model in forecasting the causality of unfavourable drug responses in patients undergoing specific therapies. Following the balancing of the data via oversampling, the total instances were divided into Train cases (85%) and Test cases (15%). The trained model was evaluated on the test cases to gauge the accuracy of predicting the causality classification. The programming was implemented after the oversampling technique was used to balance the data, the total cases were split into Train cases (85%) and Test cases (15%). Python (Ver 3.6) utilizing Keras (Ver 2) were used for the neural network.

RESULTS

In this investigation, individuals with an average age of 35.92 ± 16.9 years and an average body weight of 50.36 ± 12.8 kilograms were subjected to examination. The prevailing underlying ailments encompassed pulmonary tuberculosis (71.7%), MDR tuberculosis (11.7%), extra-pulmonary tuberculosis (8.3%), and individuals living with HIV/AIDS (8.3%). Prominent untoward responses entailed hepatitis (18.33%), peripheral neuropathy (16.67%), cutaneous eruptions (11.67%), emesis (11.67%), and pruritus (8.3%), whereas uncommon reactions such as visual impairments and psychosis were also observed. Amongst the 60 instances, 2 necessitated hospitalization and 1 culminated in fatality. Causality appraisal classified 54 instances as conceivably associated and 6 as presumably linked. The neural network that underwent training achieved an overall accuracy of 62.5% on the evaluation cases. Commonly observed adverse drug reactions were listed in Figure 1.

ıverse Reactions	Percentage
epatitis	18.33
ripheral neuropathy	16.67
ıshes	11.67
ɔmiting	11.67
hing	8.33
in	6.67
sual disturbances	6.67
ychosis	5.00
izures	3.33
ıaemia	1.67
zziness	1.67
ythema multiformis	1.67
perpigmentation	1.67
creased uric acid	1.67
yelosuppresion	1.67
al ulceration	1.67

Figure 1: Common Adverse Drug Reactions

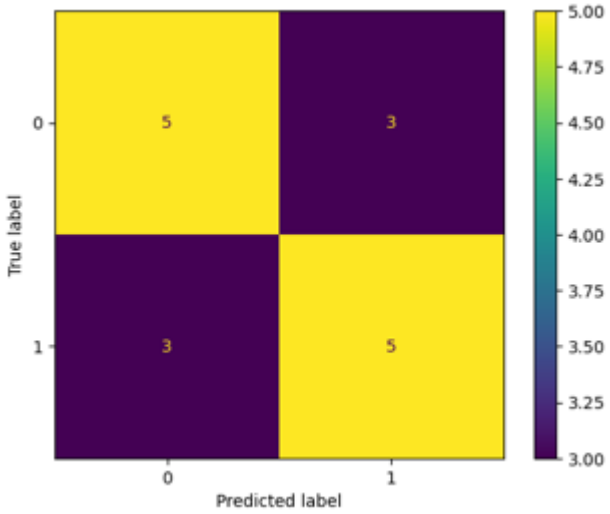

Figure 2: Confusion matrix of ADRs

DISCUSSION

The current investigation undertakes an examination of individuals encompassing a wide range of health conditions, primarily related to tuberculosis and HIV/AIDS, who underwent a treatment regimen. The average age and body weight of the participants offer contextual information about the study population, with a noticeable variation observed in both parameters.

The prevalence of pulmonary tuberculosis, multidrug-resistant tuberculosis, extrapulmonary tuberculosis, and individuals living with HIV/AIDS demonstrates the diversity of health conditions being considered. This distribution emphasizes the complexity of the study group, thereby providing insights into the challenges associated with treating individuals who have multiple coexisting health issues.

The adverse reactions reported during the investigation shed light on the potential risks and complications associated with the treatment. The higher incidence of hepatitis and peripheral neuropathy implies the necessity for careful monitoring and management of these side effects. Furthermore, the identification of less common reactions such as visual impairments and psychosis underscores the significance of comprehensive and individualized healthcare.

The instances of hospitalization and fatality within the study group are noteworthy. Although the absolute numbers are relatively low, they underscore the importance of closely monitoring individuals undergoing treatment for tuberculosis

and related conditions, particularly those with pre-existing health concerns.

The causality assessment offers a structured approach to comprehending the relationship between the treatment and adverse reactions. The classification of instances as possibly or probably linked provides a nuanced perspective on the strength of the associations, acknowledging the intrinsic complexity of attributing causality in medical contexts.

The inclusion of the performance of a neural network in the evaluation introduces a technological dimension to the investigation. The achieved overall accuracy of 62.5% on evaluation cases suggests a potential role for artificial intelligence in supporting clinical decision-making. However, further discussion and validation may be required to determine the reliability and generalizability of the outcomes generated by the neural network.

CONCLUSION

To conclude, this investigation provides valuable insights into the challenges and outcomes associated with the treatment of individuals with tuberculosis and related health conditions. The diversity of the study population, the observed adverse reactions, and the performance of the neural network contribute to a comprehensive understanding of the complexities involved in managing such cases. Further research and collaborative efforts may help refine treatment strategies and enhance patient outcomes in this context.

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