A glance at the undeniable potential of Machine Learning to curb HIV/AIDS Pandemic

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Abstract. The potential of machine learning, a specialization of the artificial intelligence domain, to potentiate the scientific research being pursued to combat the pressing medical challenges of our time can neither be denied nor overstated. HIV/AIDS, a lethal pandemic taking the lives of thousands annually, is being fought by incorporating machine learning models into the exploratory protocols aimed at reducing the associated morbidity and mortality as well as to cut down on the costs being incurred by the health care services. Adoption of such superior protocols shall allow us to keep HIV/AIDS pandemic at bay, especially in these pressing times where the global scientific community is fighting COVID 19.

Keywords: HIV, AIDS, machine learning, COVID 19.

1 Introduction

The disruptive role of artificial intelligence (AI) in each & every step of each & every pipeline currently instituted in the medical universe— may it be the exploration of the pathogenesis of an ailment⁽¹⁾⁽²⁾⁽³⁾, identification of risk factors & clinical features⁽⁴⁾, optimization of patient management protocol⁽⁵⁾, modelling of disease prognosis⁽⁶⁾ or discovery of an effective vaccine⁽⁷⁾— can neither be denied nor overstated. Even though Kulkarni S et al.⁽⁸⁾ termed AI to be "relevant to visually-orientated specialities such as radiology, pathology, ophthalmology, and dermatology", its applications in drug & vaccine discovery as well as in the optimization of patient prioritization protocols are coming out to be promising.

With key populations affected being drug addicts who inject recreational drugs, sex workers & homosexual men & lethal tuberculosis as well as hepatitis coinfections well established, HIV AIDS is termed as a "pandemic" by WHO, responsible for as many as 770 000 deaths worldwide in the year 2018, with a staggeringly high number of people, as many as 37.9 million, reported to be living with this ailment by the end of the same year. (9) With widespread stigma associated with the condition (10), HIV AIDS is a real challenge for the health apparatus to deal with.

In this literature review, we shall be exploring the applications of machine learning, a specialization of artificial intelligence, in deterring the HIV AIDS pandemic at different fronts, may it be drug discovery⁽¹¹⁾, or optimization of the patient prioritization protocol, with the end goal of decreasing the associated morbidity & mortality, as well as social stigma attributed to an HIV AIDS patient.

This is a call to all researchers to embrace the powerful & effective principles & applications of machine learning, as one of many tools, in the fight against HIV AIDS, especially in these pressing times where complete priority to the CoVid 2019 pandemic has left the HIV pandemic flank wide open, vulnerable & exploitable. (12)

2 Methods

Google scholar⁽¹³⁾ was used to search for suitable case studies. A filter for retrieving only those articles that have been published in 2020 was adopted. Key phrase adopted for the search was "hiv aids machine learning". Only peer-reviewed articles were considered. Literature reviews and preprints were not considered.

3 Case studies

3.1 Optimization of the prioritization of HIV infected patients for treatment

Rivero-Juárez A et al.⁽¹⁴⁾, by adopting a highly data-driven approach, utilized the predictive powers of machine learning to reevaluate the Spanish national strategic plan for HIV treatment by exploring such factors in HIV/HCV co-infected patients that allow them to be prioritized over others for antiviral therapy in a bid to mitigate the overall morbidity & mortality rate associated with HIV AIDS.

By exploring the massive Spanish HERACLES cohort dataset, neural networks were designed, trained & tested so as to come up with a prediction over the necessity of the initiation of the respective antiviral therapy on a patient, by taking in variables; variables that are diverse in their complexity from as simple as age & gender to as specialized as hepatic fibrosis stage, that was measured via a FibroScan (FibroScan; Echosens, Paris)-powered Liver transient elastography.

After the inevitable scaling of the input variables, the holdout procedure was used for training the neural networks where the models' performance was measured in terms of standard measures including, but not limited to, the area under the ROC curve (AUC) & accuracy. One variable: expression of irrefutable evidence of drug consumption in the previous 3 months (termed as "recent People who inject drugs") was found to be an independent variable utilized by the trained neural networks in the classification process. A splendid, high AUC of 0.802 is reported.

Utilizing such simple-to-use models, powered by machine learning, allows a physician to take an informed decision on initiating the antiviral therapy for an HIV-HCV co-infected patient.

3.2 Prediction of the survival of an HIV/AIDS hospitalized patient

In a large-scale retrospective cohort study, Yuan Z *et al.*⁽¹⁵⁾ developed an illustrative nomogram that predicts the survival probability of an HIV/AIDS inpatient to optimize the allocation of intensive-care services.

By taking in 3 724 inpatients hospitalized between the January of 2012 to the December of 2014 in the Fourth People's Hospital of Nanning, Guangxi, China & subsequently performing data dimension reduction as well as optimal predictors' selection using the least absolute shrinkage and selection operator (LASSO) method, a Cox proportional hazards regression model was designed in order to build a baseline nomogram that predicts the survival of an HIV/AIDS inpatient at 10-days & 20-days afteradmission intervals.

The obtained nomogram was tested on an external-validation cohort, with a strength of 1 987 inpatients that were admitted between the January and the December of 2015, and received an Area under the curve of Receiver operating characteristic (AUC-ROC) as high as 0.768 (95% CI 0.710–0.826) and 0.764 (95% CI 0.715–0.813) at the aforementioned two time-points.

An illustrative, simple-to-comprehend nomogram was thus developed and validated, having considerable predictive accuracy, where the Integrated Brier score was as low as 0.076 (95% CI 0.061–0.101). Such an application of machine learning allows Emergency Medicine physicians to decide which patient to be provided with immediate intensive care services.

3.3 Prediction of HIV/AIDS viral rebound

On the premise of being robust to over-fitting and noise and having the superior ability to perform multiclass classification, The Random Forest model was adopted by Kamal S *et al.*⁽¹⁶⁾ to incorporate both; The Swiss HIV Cohort Study (SHCS) and Swiss Interprofessional Medication Adherence Program (IMAP) databases into a machine learning model that predicts virological failure in an HIV/AIDS patient.

By implementing 10-fold cross-validation in order to prevent the training model from predicting the data point at hand using the future data points & by adopting Occam's Razor to choose optimal predictors to be incorporated into the training model, as much as 255 models were trained varying in the input variables they were trained on. The sensitivity was reported to be as high as 89% with small computation time required.

By adopting machine learning models along with the HIV RNA testing, the viral load monitoring can be made best suited to a respective patient's variables, reducing the health-care costs, thus.

4 Discussion

In this literature review, a concise consideration was taken over the potential of machine learning, a specialization in artificial intelligence, in curbing HIV/AIDS pandemic; Where the global health resources and channels are already strained tackling

COVID 19 pandemic, incorporating computing-friendly, easy-to-comprehend and implement protocols, having machine learning at their center, can help us in keeping the HIV/AIDS pandemic at bay, away from getting effective enough so as to wreak catastrophe.

May it be optimizing the protocol to prioritize HIV infected patients for treatment so as to effectively reduce associated aggregated mortality without imposing a burden on health resources, predicting the survival probability of an HIV/AIDS inpatient so as to decide on the appropriate management strategy to initiate or be it the realm of predicting viral reload and thus the effectiveness of the care being provided to an HIV/AIDS patient, machine learning models have come up as, if not better then, at par to the conventional gold standards. It is worth noting that such "gold standards" are not only a real burden to the global economies but also have not been successful, as of yet, to annihilate this pandemic once and for all. The situation, thus, demands for the incorporation of better strategies and machine learning is, no doubt, if not only than surely one of the major leading contenders to take the stage as the "next gold standard" in the fight against HIV/AIDS pandemic.

This literature review is but a minute glance into the scientific community's praise, subsequent exploration and consequent incorporation of machine learning in the fight against pandemics in general, particularly the COVID 19 and HIV/AIDS pandemics. Tu W *et al*⁽¹⁷⁾ utilized random forest models to explore neurocognitive impairment associated with HIV/AIDS and were able to uncover several such variables that were significantly associated with the various types of said neurocognitive development but were obscured due to the inferior analysis potential of conventional regression models. Paul RH *et al*⁽¹⁸⁾ adopted gradient-boosted multivariate regression models to build a classifier to predict the risk for "suboptimal neurocognitive development" in cases of perinatal HIV/AIDS and were able, not only to unearth novel, previously undiscovered associations between neurocognitive impairment and both; CD4 count as well as hematocrit levels, but also obtain an area under the curve as high as 90%.

5 Conclusion

Via a concise commentary that projected the undeniable potential of machine learning to be successful at all the fronts against HIV/AIDS pandemic, we provided a snapshot of the applications of machine learning in the optimization of the associated protocols and prediction of the inpatient's survival. Moreover, the potential of machine learning to uncover significant interactions influencing HIV-associated neurocognitive impairment was also exhibited. This is a call to all the scientific community to embrace and explore machine learning and subsequently incorporate it in the fight against HIV/AIDS.

6 Contributor's Statement

Both the authors contributed equally to this work.

7 Conflict of Interest

The authors declare no competitive conflict of interest whatsoever related to the material of this paper.

References

- 1. Huang Y, Liu H, Zuo L, Tao A. Key genes and co-expression modules involved in asthma pathogenesis. PeerJ. 2020 Feb 3;2020(2):e8456. doi: 10.7717/peerj.8456
- Catalina MD, Owen KA, Labonte AC, Grammer AC, Lipsky PE. The pathogenesis of systemic lupus erythematosus: Harnessing big data to understand the molecular basis of lupus. Vol. 110, Journal of Autoimmunity. Academic Press; 2020. p. 102359. doi:10.1016/j.jaut.2019.102359
- Bahado-Singh RO, Vishweswaraiah S, Aydas B, Yilmaz A, Saiyed NM, Mishra NK, et al. Precision cardiovascular medicine: artificial intelligence and epigenetics for the pathogenesis and prediction of coarctation in neonates. J Matern Neonatal Med. 2020; https://doi.org/10.1080/14767058.2020.1722995
- Farrokhi F, Buchlak QD, Sikora M, Esmaili N, Marsans M, McLeod P, et al. Investigating Risk Factors and Predicting Complications in Deep Brain Stimulation Surgery with Machine Learning Algorithms. World Neurosurg. 2020 Feb 1;134:e325– 38. doi:10.1016/j.wneu.2019.10.063
- Blasiak A, Khong J, Kee T. CURATE.AI: Optimizing Personalized Medicine with Artificial Intelligence [Internet]. Vol. 25, SLAS Technology. SAGE Publications Inc.;
 2020 [cited 2020 Jun 18]. p. 95–105. Available from: http://journals.sagepub.com/doi/10.1177/2472630319890316
- 6. Chicco D, Jurman G. Machine learning can predict survival of patients with heart failure from serum creatinine and ejection fraction alone. BMC Med Inform Decis Mak. 2020 Feb 3;20(1):1–16. https://doi.org/10.1186/s12911-020-1023-5
- Chaudhury S, Duncan EH, Atre T, Dutta S, Spring MD, Leitner WW, et al. Combining immunoprofiling with machine learning to assess the effects of adjuvant formulation on human vaccine-induced immunity. Hum Vaccines Immunother [Internet]. 2020 Feb 1 [cited 2020 Jun 18];16(2):400–11. Available from: https://www.tandfonline.com/doi/full/10.1080/21645515.2019.1654807
- 8. Kulkarni S, Seneviratne N, Baig MS, Khan AHA. Artificial Intelligence in Medicine: Where Are We Now? Vol. 27, Academic Radiology. Elsevier USA; 2020. p. 62–70. doi:10.1016/j.acra.2019.10.001
- 9. WHO | Data and statistics [Internet]. [cited 2020 Jun 14]. Available from: https://www.who.int/hiv/data/en/
- 10. Steenberg B. Patients and Personhood: Perceptions of HIV in Mozambican Immigrants in South Africa. Med Anthropol [Internet]. 2020 Apr 2 [cited 2020 Jun 14];39(3):211–24. Available from: https://www.tandfonline.com/doi/full/10.1080/01459740.2019.1677646
- Kneller DW, Agniswamy J, Harrison RW, Weber IT. Highly drug-resistant HIV-1
 protease reveals decreased intra-subunit interactions due to clusters of mutations.

- FEBS J [Internet]. 2020 Jan 23 [cited 2020 Jun 16];febs.15207. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/febs.15207
- 12. Shoptaw S, Goodman-Meza D, Raphael ·, Landovitz J. Collective Call to Action for HIV/AIDS Community-Based Collaborative Science in the Era of COVID-19. [cited 2020 Jun 16];1:3. Available from: https://doi.org/10.1007/s10461-020-02860-y
- Google Scholar [Internet]. [cited 2020 Jun 18]. Available from: https://scholar.google.com/
- 14. Rivero-Juá Rez 1 A, Guijo-Rubio D, 2 ID, Tellez Id F, Palacios R, Merino D, et al. Using machine learning methods to determine a typology of patients with HIV-HCV infection to be treated with antivirals. journals.plos.org [Internet]. 2020 [cited 2020 Jun 14];15(1). Available from: https://doi.org/10.1371/journal.pone.0227188
- 15. Yuan Z, Zhou B, Meng S, Jiang J, Huang S, Lu X, et al. Development and external-validation of a nomogram for predicting the survival of hospitalized HIV/AIDS patients based on a large study cohort in western China. Epidemiol Infect. 2020;148. https://doi.org/10.1017/S0950268820000758
- 16. Kamal S, Urata J, Cavassini M, Liu H, Kuoyos R, Bugnon O, et al. Random forest machine learning algorithm predicts virologic outcomes among HIV infected adults in Lausanne, Switzerland using electronically monitored combined antiretroviral treatment adherence. AIDS Care Psychol Socio-Medical Asp AIDS/HIV. 2020; https://doi.org/10.1080/09540121.2020.1751045
- 17. Tu W, Chen PA, Koenig N, Gomez D, Fujiwara E, Gill MJ, et al. Machine learning models reveal neurocognitive impairment type and prevalence are associated with distinct variables in HIV/AIDS. J Neurovirol. 2020 Feb 1;26(1):41–51. doi:10.1007/s13365-019-00791-6
- 18. Paul RH, Cho KS, Belden AC, Mellins CA, Malee KM, Robbins RN, et al. Machine-learning classification of neurocognitive performance in children with perinatal HIV initiating de novo antiretroviral therapy. AIDS [Internet]. 2020 Apr 1 [cited 2020 Jun 18];34(5):737–48. Available from: http://journals.lww.com/10.1097/QAD.000000000002471