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A Survey of the Various Methods and Models Used to Detect Long COVID

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***Abstract*—Long-COVID or post-COVID is a phenomenon where people who have recovered from the COVID-19, suffer persisting symptoms for more than 4 weeks after the confirmed case of COVID-19 and they can last for months. Approximately 20% of the people affected by this Coronavirus disease (COVID-19) are suffering from mid and long term effects known as the Long COVID and it can affect multiple organs in the body and this can lead to death. To date, different studies and researches have been undertaken to understand about the Long COVID and make robust estimates on the predicting factors, symptoms and also to assess the various long term effects on the patients affected by it. Based on the available research articles and the papers published in mainstream journals on Long COVID, this survey paper aims at analyzing various methods and Machine learning models used to detect and predict Long COVID, to help clinicians and researchers working on early diagnosis of Long COVID.**

***Index Terms*—Long COVID, COVID-19, Sequelae, Machine Learning models, Predictive factors, Symptoms, Correlation**

I. Introduction

Coronavirus is a contagious disease which emerged in December 2019 in the City named Wuhan in China.The infectious disease caused by SARS - COVID- 2 was formally called Coronavirus disease-19 or COVID-19 by the World Health Organization on February 11, 2020 [20]. It affects the nose, sinuses and the throat of the upper respiratory tract and also the windpipe and lungs of the lower respiratory tract. The infection is risky for individuals of all ages, but people aged 60 years and those with any kind of chronic medical condition are more prone to the disease. The viruses are constantly changing and different variants are now spreading all over the world, which are found to be more deadly than the original virus. The period of incubation for COVID-19 is estimated to be up to 14 days [6]. The symptoms and the severity of the disease may not be same for everyone and it's range of illness varies from no symptoms to symptoms with severe pneumonia, difficulty in breathing, multi organ failure and this can even lead to death in some patients [17]. Out of the affected people, 80 % had mild to moderate symptoms and they were able to recover from it within 12 weeks. But among the patients with severe symptoms, it can last longer and the 5 % developed a chronic illness [14] and they required medical attention [26].

A. COVID-19 Signs and Symptoms

The most common symptoms of COVID-19 are as follows [15]: Fever, loss of smell/taste, headache, dry cough, congestion, shortness of breath, sore throat, fatigue, runny nose, sore throat, chest pain, joint pain, nausea, loss of appetite and diarrhea. The main abnormality that is found in the X-rays of patients infected with the virus is found to be bilateral multifocal opacities [11], this indicates that the virus has caused a serious infection in the lungs. In some people it has even caused loss of vision [5]. Although it is considered to be a pulmonary disease, different researches have now shown that it can affect other organs and can lead to cardiac, dermatologic, hematologic, hepatic, neurologic, renal and other complications [1].

B. Long COVID

When the effects of COVID-19 in patients persist for weeks or, even months, then it is described as 'Long COVID' and the health issues related to it are called 'post-COVID-19 conditions'. Long COVID is popularly called as post-COVID-19 syndrome and the experts call it as post-acute sequelae of COVID-19 (PASC), chronic COVID syndrome (CCS), or post-COVID-19 condition [22].

Long COVID is a word created by patients and was first used by an archaeologist named Elisa Perego of the University College London [19]. No single, clear cut definition exists for Long COVID and different organizations have defined it in different ways based on the studies and the research. The popular definition given to long COVID is, it's a condition that lasts for more than 12 weeks, even though there are people with symptoms that can last more than eight weeks. While the WHO defines Long COVID as a phenomenon that can last for minimum 2 months and that can't be explained clearly by a diagnosis [22].

Long COVID/PASC is a multi-system illness and the symptoms of patients can vary. Symptoms can be the same or they

can vary from what they had during the initial phase of COVID when compared to the ones they have after the Polymerase chain reaction (PCR) value becomes negative. Anyone affected with COVID-19 can have long COVID, even though they were not having any symptoms or were only having mild symptoms. The symptoms can be physical, cognitive, pulmonary and also related to mental health. As a result, day to day activities of the patient get affected [25].

II. Choice of Papers for Survey

There are only very few available studies on Long COVID that helps the clinicians understand and to work on the treatment. Different studies have focused to find its predictive factors and how they affected the different organs in the body. The main focus of this survey was to help the doctors find out who is at increased risk of experiencing Long COVID. Consequently, to that end, papers on population-based estimates, papers assessing different demographic factors, symptoms and severity of long COVID were chosen in such a way that it helps us to realize how it affected the daily lives of the people. Since our focus was mainly on the diagnosis, prediction and also prognosis, most of the early research papers were making use of artificial intelligence and machine learning. This survey has included almost 12 research papers published in different mainstream journals relating to biomedical, infectious diseases, research articles and also the technical papers published by the world's leading publishers which include the AI and ML models for the prediction and also for the detection tasks of PASC.

A. Survey of Papers

A probability survey based on the population in the state of Michigan was conducted considering the adults($\geq$ 18) affected with COVID-19, to estimate what is the prevalence and the major factors that correlate to PASC infection. Patients who got COVID before 15th April (June-December 2020) were considered. Almost 629 patients of the total 2000 completed the survey. To find the Long COVID prevalence, different Sociodemographic factors like 4 different age groups between the age of 18-64 and 5th age group considering the patients above the age of 65, gender of the patients (male/female), their race, annual income were considered. The factors relating to clinic include checking preexisting conditions like hypertension, cancer, asthma, liver disease, diabetes, heart disease, cerebrovascular disease, kidney/liver disease, physical or psychological disability and the symptoms that persisted for more than 30 or more than 60 days after the recovery from COVID-19. Smoking status of the patients, severity of symptoms reported by them, and their hospitalization status was also verified. To get the prevalence ratio, used modified Poisson regression. Of the total taken predominantly 56.1 % were females, aged $\geq$ 45 years (68.2 %). 30 and 60 days COVID -19 was found to be more (52.5 % and 35.0 %). It was found that 30-day COVID-19 was having a higher prevalence of 2.25 times when compared to the 60-day COVID-19 when the patient was having severe symptoms. So patients with severe initial symptoms are prone more to PASC when compared to patients with mild to moderate symptoms. But the paper didn't discuss about the long-term consequences of PASC [8].

Another study based on the electronic records of 437 adult patients of the Mayo clinic in Florida was conducted to find what all are the common symptoms of PASC and whether they have any correlation with the severity. Kruskal-Wallis rank sum method and X^2 test were used to understand and find the period of duration for recovery. The results have shown that the most common symptoms of PASC are fatigue, poor sleep quality, anosmia, dysgeusia, and dyspnea. It has also shown that the predictive factors for PASC are women and patients with psychological symptoms. But the study here didn't consider the lab results of patients and how they are correlated to the disease [12].

Another survey, which was based on the COVID Symptom Study app took 4,182 COVID cases from the US, UK, and Sweden regions. Long COVID was defined by trouble sleeping, difficulty breathing, headache, and loss of smell, with other characteristics such as age, gender, and body mass index (BMI). A Random Forest Prediction model was created based on the combination of symptoms during the initial week of COVID-19, personal characteristics and chronic condition and the result was found as age and no of symptoms in the first week as the main predictors. The major limitation of this research work was that it considered only the self-reported survey of the patients and did not include the clinical data of the patients [23].

Similarly, in another study of 290 outpatients participated in the telemedicine program of Emory Healthcare and the survey was to find the symptoms, severity of the disease, and their quality of life. They performed Bivariate and multivariate analyses to assess predictors of the symptoms. The survey collected general information, experience with COVID-19, severity, persisting symptoms, how physically, mentally and emotionally it affected quality of life, and the hospitalization status. To understand whether the symptoms are related to the severity at the initial stage they made different categories relating to respiratory like dyspnea, dry cough, joint pains, neurological and dysgeusia. The most common comorbid conditions were found as obesity, Hypertension and asthma. It was discovered that the severity of the early symptoms could indicate the risk of long-term illnesses, which suggests that there are chances for acute inflammation. The work was focused only on the self-reported survey and did not consider the current status of the patients [16].

A study in Arizona CoVHORT (a study of the SARS-Cov-2 epidemic on a group of people and its consequences) took a total of 303 non-hospitalized patients and also the participants of COVID-19 studies and the survey was done at 3,6,9 and 12 months of post-baseline. The comparison was done using chi-square, t-test, or non-parametric equivalents, and the statistics were computed by categorising on PASC status. Multiple Imputation using delta adjustment was used to consider the potential dropout of patients in the survey and

the stress/anxiety was considered as the pandemic's impact. According to the research, the median number of symptoms is three and those symptoms are fatigue, brain fog and anxiety. The study has shown that people with lesser education, women, those who have at least one pre-existing medical condition and with greater illness severity at the initial stage were found to be more prevalent to PASC, but all these were only based on self-reported surveys from the non-hospitalized patients [3].

CT scan of patients taken on the six month after recovery from COVID-19 pneumonia was used to evaluate the injury to the lungs in Italy and this was accomplished by collecting the CTs of 118 patients in a hospital in Rome. To detect late sequelae, CT qualitative data such as the semi-quantitative score to know the severity of the Lungs and CTs taken of the chest were evaluated. To predict fibrosis like changes Univariable and multivariable logistic regression have been tried on clinical parameters and on the radiological attributes. Based on this research main predictors for fibrosis were found as males(gender), cough, lymphocytosis, and lung volume at QCCT analysis. As fibrosis-like changes are visible in CTs only after 6 months, the early stage diagnosis of PASC is not possible by using this study [4].

To classify Long COVID and also severe COVID conditions, healthy people's blood and isolated peripheral blood mononuclear cells, patients with mild symptoms, and severe symptoms, also individuals having PASC are analyzed. Random Forest Model could determine the critical cytokines, which aided in the development of a system to categorize based on the immunity when patients are having higher symptoms of PASC. The main drawback of the study is that it considered only the cytokines for the classification, no other major features like symptoms of COVID-19 were considered in the study [18].

Another study, to calculate the consequences of having post COVID features and compare it with that of influenza, collected 273,618 patients' electronic health records in the USA. Considered 58 variables, including demographics, health condition, and habits of the patient. The Cox regression model and the Kaplan Meier analysis were employed to match the scores of patients with long COVID and influenza. The incidence, features were found to be more common with long COVID than with influenza and they were shortness of breath, tiredness, sore throat, headache, depression, myalgia and cognitive symptoms. Research has shown that patients with long COVID features in 3-6 months were most likely having such features in the first 3 months. Patients with severe COVID-19 sickness, women, and young persons were shown to be at higher risk. This research work has only considered the self-reported surveys of the patients and was not considering the test results [24].

A study of the recovered patients of Jammu Kashmir was done and their details were collected like demographics, symptoms and severity which showed that heart disease is the most common long-lasting complication of COVID-19 patients. A binary classifier based on a stacking ensemble modelled with a deep learning model was used to predict heart disease. The major drawback of this work is that it was focusing only on the general symptoms and demographics and is not based on any clinical results of the patient [7].

In another study to find COVID-19 risk factors linked to the occurrence of long-term COVID, details of 277 patients were collected in Spain. A multiple logistic regression model was employed to determine which risk factor was the most important (symptoms) of COVID-19. The common symptoms of PASC were found in the study as fatigue, and dyspnea and found that no baseline clinical features, comorbidities, demographics, or severity is behaving as independent predictors of PASC and this study was also focusing only on the self-reported surveys of the patient [13].

B. Machine Learning Models

Artificial Intelligence (AI) is the broad field that permits machines to mimic human behavior or these are the systems that can perform complex tasks in the same way in which humans solve the problems. Machine Learning (ML) is a subset of AI that trains a machine how to learn. Over the years, AI and ML have been in use in numerous fields like object detection, health care industry, fraud detection, finance, image processing etc. Since they are associated with increased accuracy and computation level, it has helped the medical field in many ways like in diagnosis, prediction, and the prognosis of different diseases [21]. AI and ML solutions have widely helped in the field of COVID-19. Most of the research related to COVID-19 is based on AI. Machine Learning includes Deep Learning as a subset and it has been found that research on COVID-19 in the initial period was found to be mainly based on the Deep Neural Network [2]. This mainly helped in the diagnosis, prediction, vaccine availability, and prognosis related to COVID-19.

A survey was conducted to find the models used in different papers related to the diagnosis and prediction of COVID-19. The PASC occurrence ratio was calculated using a Modified Poisson regression model the results have shown that patients with severe symptoms showed almost 2.25 times more prevalence of Long COVID. Whereas in [12], to find the persistent symptoms, for continuous measures, the Kruskal-Wallis rank sum was used, and for categorical values, the X^2 test was used and it was found that on a clinical data of 437 patients, common symptoms were tiredness (75.9 %), anosmia (56.8 %), sleep deprivation (60.3 %), dysgeusia (55 %), dyspnea (54.6 %). [23] used Random Forest Prediction Model and the features considered were symptoms in the first week of COVID-19, individual traits and comorbidities. For the considered model strong predictors were Age (29.2 %) and the amount of symptoms experienced in the first week (16.3 %). To make it simpler for clinical authorities, a Logistic Regression Model was also used in the same paper with number of symptoms, age and sex as the features and it was shown that the main predictor was the prominent 5 symptoms in 1st week. Bivariate analysis and Multivariate analysis were performed for each category of symptoms, severity and other

TABLE I
COMPARISON OF SURVEYS THAT USED DIFFERENT METHODS AND MACHINE LEARNING MODELS IN RESEARCHES RELATED TO LONG COVID

Methods/ ML Model	Features	Number of Patients	Result and Performance of the models
Modified Poisson regression [8]	Sociodemographic factors, clinical factors,symptoms of post-COVID condition	629	Patients with severe symptoms showed 2.25 times more prevalent to Long COVID
Kruskal-Wallis, X^2 test [12]	Age, sex,persistent symptoms	437	Common symptoms: fatigue (75.9%), poor sleep quality (60.3%), anosmia (56.8%), dysgeusia (55%), dyspnea (54.6%) Women and patients with psychological problems are more prone to PASC
Random Forest Prediction Model and Logistic Regression Model [23]	No. of symptoms during first week,Age, sex, comorbidities	4182	Strong predictor for PASC was found to be 5 symptoms in 1st week
Bivariate chi-square Analysis, Multivariate Logistic Regression [16]	Symptoms, severity, basic demographics	290	Predictors of PASC: Common comorbidities : Obesity, Hypertension, asthma Symptoms: Fatigue(20.3%), Dyspnea(14.1%)
Chi-square, t-tests, Wald CIs, distributed free CIs [3]	Gender, Age, Symptoms, severity	303	Predictors of PASC: Females, Pre-existing chronic condition Symptoms: seasonal allergies(42%), asthma(16%), hypertension(15%)
Univariable, Multivariable logistic regression analysis [4]	Demographics, symptoms,Lung Severity Score (LSS) of patient, Chest CT	118	Main predictors to find PASC: Male, cough, lymphocytosis, and lung volume at QCCT analysis
Random Forest Model classifier [18]	Different cytokines	224	Model Accuracy : 96% Strong predictors for PASC: Cytokines (IL-6,IL-10) High values of IL-6,IL-10 then patient will have severe COVID
Kaplan Meier analysis, Cox proportional hazard model [24]	Demographics, health condition, habits of patient	2,73,618	Symptoms more frequently reported in Long COVID when compared to influenza with excess incidence of 16.60% and hazard ratios between 1.44 and 2.04
Decision trees, support vector machines,random forest, artificial neural networks,a Binary classifier based on a stacking ensemble [7]	Demographics, Severity of COVID-19, Symptoms	180	Binary classifier based on stacking ensemble modeled with deep neural networks was having higher accuracy, Model accuracy: 93.2% to predict heart disease
Multiple Logistic Regression [13]	Demographics, comorbidities	277	Common symptoms of PASC was found as: Fatigue,Dyspnea No clinical features behave as independent predictors

covariates in [16] and it was found from the analysis that the common comorbidities are Obesity, Hypertension, asthma with symptoms: Fatigue(20.3 %), Dyspnea(14.1 %).To calculate the statistics related to PASC, chi-square and t-tests were done [3]. To find the Confidence Interval of Long Covid and the prevalence, binary variables and medians used Wald CI and distributed free-CIs respectively. The result has shown that the females are more prevalent to Long COVID than males(73% versus 63%) In [4], Multivariable logistic regression was performed on clinical, radiological and combined models/parameters and the score to find the severity of lungs and the well-aerated lung capacity from the CTs of the chest were found to be predictive of fibrosis-like alterations. To predict a patient belongs to severe COVID-19 or PASC in [18], a random Forest, multi-class Random Forest and Binary PASC random forest Model classifier was used and they considered different cytokines as the features and the random forest model could determine the strong predictors as Cytokines (IL-6, IL-10) and high values of IL-6, IL-10 were showing severe COVID. Similarly, to estimate the risk of long COVID features and to compare that with influenza [24], to compare patients of PASC and influenza analysis was done by using Kaplan Meier technique and the Cox proportional hazard model were utilised and it showed that features/ symptoms more frequently reported in Long COVID and were having an excess value of occurrence of the event (16.60 %) and hazard ratios was set between 1.44 and 2.04. Deep neural networks are used to model a binary classifier based on a stacking ensemble

in [7] to predict heart disease in post-COVID-19 and the model was validated against the random forest, decision trees, support vector machines (SVM), artificial neural networks. The new model developed has showing an accuracy of 93.2 %, precision 95.24 %, and recall 92.05 %. To evaluate the disease severity, chi-2 test was done in [13] and the risk factors related with Long COVID were discovered using Multiple Logistic Regression and it was found that common symptoms were fatigue and dyspnea, with no clinical features behaving as independent predictors. Table 1 shows a comparison of the different surveys which used different statistical methods and ML models detect Long COVID.

III. Types of Long COVID

There are mainly 3 types/ categories of Long COVID as shown in Figure 1:

- First Category: COVID-19 causing direct damage to the cell. The virus causes the cell damage and the patient suffers or shows symptoms of that.
- Second Category: Symptoms of Chronic Hospitalization. Caused when the patient is hospitalized for weeks and is in the hospital bed or the ICU. This creates muscle weakness, brain dysfunction and post-traumatic stress disorder-like syndrome.
- Third Category: Symptoms appearing after COVID-19 recovery. New symptoms start appearing in the patients because of the autoantibodies in the blood and some of them starts reappearing due to the presence of SARS-COV-2 RNA levels and also the Type-2 diabetes.

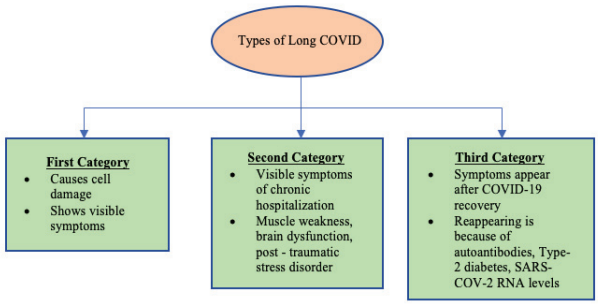

Fig. 1. Types of Long COVID

IV. Comparison Results on Long COVID

The comparison of the different surveys has shown that the predictive and the significant symptoms of Long COVID can be identified by different statistical methods and the detection of the Long COVID can be performed using different Machine Learning models. To find the predictive factors of Long COVID, the future researches can be based on statistical hypothesis test like Chi-square test for the categorical variables, t-test for continuous variables and Kruskal-Wallis for both the continuous and ordinal level variables. Whereas the Cox proportional hazard model can be a best option to find the effect of different symptoms of Long COVID as it can take both continuous and binary predictors. Even though different researches have used different Machine Learning models, the best model for the detection of Long COVID was found from the comparison as Random Forest Model classifier as it performed well with an accuracy of 96%. But to predict the effects of Long COVID the best option is to choose a binary classifier based on stacking ensemble modeled with deep neural network.

Analysing the recovered patients has shown that females [10] and the disease's severe psychological impact is the predicting factors of Long COVID/ PASC as they are having the highest dependence towards PASC. The studies have shown that patients who at least have one pre-existing condition and those who were having severe initial symptoms at the initial phase of COVID-19 are more prevalent to Long COVID when compared to a patient with mild to moderate symptoms [9]. Another important predictor of Long COVID is growing age, as well as the number of symptoms in the first week of COVID-19, with a patient who has more than 5 different symptoms in the first week being more prone to have symptoms lasting for a longer period. The most common comorbid conditions were found as obesity, hypertension and asthma and the most common long-lasting complication was found as heart disease.The main symptoms of Long COVID are found as:

- Fever
- Poor sleep quality
- Anosmia
- Dysgeusia
- Dyspnea

V. Conclusion and Future Scope

Almost 10 to 30% of patients who experienced COVID-19 were having persistent symptoms, even if they were not sick or were having symptoms during the initial period of COVID-19. This survey was done to analyse the state of the art in the prediction of Long COVID by using different Machine Learning models and to know what all factors can be taken as the features of a model to improve its performance to help the clinicians. The comparison of survey has shown that the Random Forest model can be the best choice to detect Long COVID and the Binary classifier based on Deep Neural Network can be used to predict the effects of different diseases that occur because of Long COVID. Although the predictive factors can be found out by the chi-square, t test and another major option is used to use Pearson correlation to find how each feature is correlated and are significant to Long COVID. The major drawback found in most of the research papers was that the study focused on the self-reported surveys of the patients, who were not even hospitalized.

Thus, the future researches can be based on the early diagnosis of Long COVID, lab test results of the patients obtained during the initial week of COVID-19 can be used rather than using the self-reported surveys as the symptoms can vary from person to person and clinicians need more reliable sources. The initial diagnosis of Long COVID with

the help of the lab test results of the patients during the period of acute COVID-19 can help the medical practitioners to treat the patients at the early stage, thus reducing the risk of the development of chronic conditions which can lead to death.

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