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Review of Chronic Inflammation and long term effects on health using Machine Learning Algorithms

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Abstract—The purpose of this review is to find how today's generation impacted with chronic inflammation and its effects on health and long-term diseases using Machine Learning Algorithms. These diseases are found to be appeared after long time suffering with chronic inflammation. By detecting it early and taking lifestyle changes and healthy diet could potentially avoid the diseases like diabetes, cardiovascular diseases, cancer, arthritis, and bowel diseases. Autoimmune disease symptoms can be minimized by identifying inflammation levels and by taking precautionary measures at any stage of the patient. There are various inflammation markers to detect inflammation in the body by simple blood tests like CRP, ESR which are inexpensive and provide early disease detective mechanisms. These reports can be input to Machine Learning algorithms and train the system to help the patients to identify inflammation levels and alert them to take appropriate actions to prevent further damage from diseases on human organs.

Keywords— Machine Learning, algorithm, Inflammation, Autoimmune.

1. INTRODUCTION

A. Background

Inflammation is two types, acute and chronic. Acute inflammation persists for short term, but chronic inflammation remains for long term in the body. Acute inflammation is required for the body to heal the injuries whereas chronic inflammation causes serious health hazards and lead to chronic diseases like cancer, heart diseases, diabetes, arthritis, allergies, psoriasis, and bowel diseases [3]. Higher level of inflammatory markers values like serum CRP and interleukin 6 are found with these health conditions. These tests are predictors of coronary heart diseases. As Galland says “Prior work has shown that elevations of high sensitivity CRP predict future development of diabetes and hypertension more accurately than body mass index (BMI)” [1].

B. Problem:

According to Chalkiadaki and Guarente “Research indicates that diet plays a significant role in regulating chronic, systemic inflammation” Crimarco et al. (2019) [1]. In due course Inflammation can damage good cells, and tissues, then organs. These can reflect as chronic diseases like various types of cancers, cardiovascular diseases, arthritis, diabetes, bowel diseases, respiratory disorders, and Alzheimer’s [2]. Typically avoiding inflammatory foods shows very good improvement in disease symptoms. At the same time including healthy foods in diet like fresh fruits and vegetables, good fats, lean meats, and proteins will benefit the body with various nutrients, minerals and relieve the pains and other disease symptoms [3]. Reactive foods have huge impact on autoimmune conditions especially the pains will be relieved heavily by avoiding these foods. These diseases will not erupt overnight, rather they get developed over the years due to poor diet and lifestyle habits, stress, and lack of sleep. Spondyloarthritis is a class of disorders caused by inflammation in joints and spinal column. Young adult age group faces this disease, and it can contribute to significant physical disability and the chances of recovery could diminish in later stages. Early detection of this disease is important to provide effective treatment to patients [4].

C. Contribution:

Inflammation markers need to be addressed and take measures in lifestyle interventions to avoid or minimize the symptoms of life-threatening diseases. Machine Learning techniques help to simplify the process of understanding inflammation levels and required measures to be taken, which will help the society at large to reduce the unnecessary expenses of health issues and to avoid going through painful symptoms. By considering the side effects of medicine usage for long term like corticosteroids to treat chronic diseases, changing diet and lifestyle habits are far better to weigh. In this process Machine Learning Algorithms will be helpful to diagnose and predict the inflammation levels based on Electronic Health Records of patients.

II. MACHINE LEARNING DEFINITIONS

Artificial Intelligence (AI) is the area of computers which will perform jobs like humans can perform, such as image identification and categorization, recognizing languages and translating to other language, and providing solutions to the specific problems [10, 33]. Machine learning (ML) is a branch of AI [34]. ML can read the complex medical images. ML algorithms are used for diagnosis and to perform challenging tasks like analyzing X-ray images, blockage detection, any additional growth detection in cells and organs as part of cancer diagnosis, breast carcinoma detection, malignancy identification with MRI and identifying brain mental state to diagnose neurological disorders. ML algorithms input with data set to learn data, then apply it to make a prediction. ML is used for speech recognition, translating languages, navigation of vehicles, and product recommendations. The writers explain by saying, "The new algorithms, combined with substantial increases in computational performance and data, have led to a renewed interest in machine learning". Few common terms in ML are Classification, Model, Labeled Data, Training, and Validation set, Testing, Node, Layer, and Weights. ML algorithms are classified as supervised, unsupervised, and reinforcement learning [5, 32]. Deep learning is part of ML techniques based on neural networks with many layers [11]. Classification is the most important part of ML algorithms in medical systems, for example the diagnosis of a disease, in which the attributes can be of different disease states or possible therapies [27]. Chronic inflammation causes certain body parts recurrently inflamed [28].

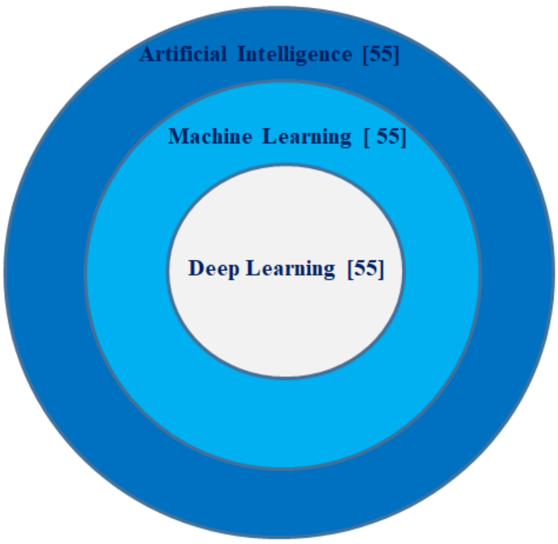

Fig 1. Venn diagram to display relationship between Artificial Intelligence, Machine Learning and Deep Learning [55]

The commonly used Supervised Machine Learning algorithms are [6, 56]:

- Support Vector Machines [36, 56]
- linear regression [56]
- logistic regression [37, 56]
- naive Bayes [56]
- linear discriminant analysis [38, 39, 56]
- decision trees [40, 41, 56]
- k-nearest neighbor algorithm [42, 56]
- Neural Networks (Multilayer perceptron) [43, 56]
- Similarity learning [44]

There are 2 comprehensive techniques in UL are NN and Probabilistic Methods. The commonly used unsupervised learning algorithms are [7]:

- Clustering [7]
  - hierarchical clustering [45]
  - k-means [46]
  - mixture models [7]
  - DBSCAN [7]
  - OPTICS algorithm [7]
- Anomaly detection [7]
  - Local Outlier Factor [7]
  - Isolation Forest [7]
- Neural Networks [7]
- Approaches for learning latent variable models such as [7, 56]

Reinforcement Learning is a domain of ML focuses on how the agent must perform operations in the application to produce better and efficient outcome using sequential rewards [35, 8]. RL is used in many fields such as games, management study and statistical analysis. In the management study RL referred as neuro dynamic programming. Fundamentally RL is designed as Markov decision process (MDP) [8].

III. RELATED WORK

A. Existing Research:

Crimarco et al. (2019) adapted baseline statistics to derive variables like categorical and continuous. The relationship between Dietary Inflammatory Index scores and blood count report using multiple linear regression analysis. Bivariate and Quantile analysis were used, and attributes are adjusted in this model. According to Ruiz-Canela et al., "The DII appears to be an effective tool for measuring the relationship between diet and inflammation with chronic diseases". According to this study the quality of diet will be useful to reduce chronic inflammation [1].

Faleiros et al. (2020) studied that AI method used in classification tasks like melanoma, differentiation of smoking conditions based on DL with MRI, classifying of ulcers, evaluating of cancer, respiratory disorders, and fractures. Various predictive models created in statistics using multiple approaches and attributes. According to this study machine learning based models have restraints hence evaluating the performance of these techniques for specific application is required. Haralick texture attributes were calculated using a graylevel co-occurrence matrices (GLCMs). Tamura texture attributes were calculated with 16 rules, for 18 attributes. SVM, MLP, and IBA methods used toward attribute selection. MLP classifier gave best results of sensitivity, specificity, accuracy to 100%, 95.6%, 84.7% respectively. Results conclude that ML methods (MLP being the best) have potential to recognize sacroiliac joints (SIJs) in axial spondyloarthritis sufferers and to detect active inflammatory sacroiliitis on MRI STIR sequences [4].

Pieszko et al. (2018) studied to predict short-term outcomes of Acute Coronary Syndrome (ACS) to evaluate ML algorithms using blood spatter inflammatory biomarkers since increased systematic and local inflammation is significant in pathophysiology of ACS. They have analyzed 6769 hospitalizations of patients with ACS. With binary classification methods, its observed that Significant coronary lesion (SCL) and survival rates are 73% and 1.4% respectively. Supervised learning algorithm models used to train and predict this type of classifications. Dominance-based rough set approach was the best model and this classifier used to identify diabetic conditions, BP measurements and blood clotting time/disorders to find the patient survival rates in the hospital. To predict and improve ACS results neutrophil count inflammation marker is significant factor, and this type of inexpensive markers are emerged in medical industry which are useful in risk classification and its optimal management [47, 48]. According to this study ML models can predict ACS and deliver accurate results [9].

Tabib et al. (2020) discussed how ML techniques implemented in research of inflammatory bowel disease (IBD) with bigdata. ML algorithms enable patient classification in different groups and predict the status of disease and therapeutic response to customize and provide better therapeutic solutions for patients. ML algorithms can detect patterns by classifying patients based on screening of a patient's medical records. Bigdata, large medical datasets, ML algorithms and medical related tools have explored biological information relevant to IBD and are helpful to find causative factors in individual patients. Deep Learning (DL) algorithms are useful for making predictions but also being helpful to provide apprehension of biomedical data. Disease monitoring is crucial by monitoring different biomarkers like fecal calprotectin, serum CRP, colonoscopy, abdominal ultrasound, and MRI [49,50]. ML used for personalized predictions which will improve medical care and outcomes with substantial reduction in healthcare expenses. ML models, like random forests, are used widely in microbiome research because of easiness, and excellent feature selection [10].

Yu et al. (2018) studied Hand-foot-mouth disease which is infectious. Cytokines are responsible in inflammation, immune and viral infection responses which will impact the infectious disease largely. ML algorithm used to classify Cases according to the cytokine profiles because inflammation causes due to cytokines accumulation. Cell-mediated inflammation is linked to central nervous system (CNS) of multiple sclerosis (MS) patients. Diagnosing the HFMD incidents and regulating the affliction is critical to intercept HFMD epidemic by having better understanding of inflammatory profiles. In Results, HFMD presented in adult patients with dysregulation of cytokines. According to the analysis of this study some of the cytokines have positive but some have negative correlation. By using Random Forest ML algorithm cytokine profiles are classified into HFMD and control classes with good accuracy. According to the findings "Cytokine expression was correlated to the enteroviral infection, genotype and clinical presentation. The inflammatory profiles can be developed as markers to identify HFMD cases using ML algorithm" [13].

Kegerreis et al. (2019) studied to diagnose systemic lupus erythematosus (SLE) using RNA species data. ML classification algorithms used for generating gene related data. GLM, KNN and RF algorithm classifiers are used to segregate active and inactive SLE sufferers to evaluate the efficacy of data. These models are trained on data sets separately and performed the test. RF algorithm classifier being best method to approach SLE diagnosis. According to this study, RNA species data as input to ML algorithms especially RF algorithm classifiers are performing with high accuracy to classify and analyze SLE status in patients [14].

Kim & Tagkopoulos (2019) reviewed ML methods used in rheumatology department. Feature Engineering is used to transform the no. of joints with swellings and the inflammation marker ESR into a feature which could assess the disease status in RA patients. According to this study that customized treatment plans can be provided to patients to get satisfactory results by collaborating and working as a team with healthcare practitioners, scientists, ML analysts, and administration personnel in clinical applications which will provide the better prognosis in RA patients [17].

Stafford et al. (2020) reviewed ML algorithms to diagnose and find medical problems of autoimmune conditions patients. SVM and RF algorithms are used widely on common diseases data sets like MS, RA and IBD. Resampling procedures and testing the ML algorithms separately are important factors. Omics [34] data (patient medical profiles) as input to ML algorithms will provide the diagnostic information of autoimmune conditions. Support vector regression was used mostly in disease monitoring and management. Single Nucleotide Polymorphism or Genome-wide association studies data is used widely to predict autoimmune conditions risk factor. Majority of the models achieved good performance (accuracy, AUC, Sensitivity, and Specificity to 81%, 0.95, 82, 84 respectively) using classification algorithms based on factors like disease, control [18].

Rush et al. (2019) reviewed ML applications to analyze complex data for physiological monitoring. ML algorithms are used for monitoring on clinical data, which will be trained and validated to learn. False alarms and abnormal values happen due to alarms are not designed sufficiently tailored to individual patients, whereas ML can create more personalized medicine. ML can analyze individual Electronic Health Record (EHR) data and provide suggestions as to the underlying pathophysiological events that have produced these anomalies. ML approaches reduce human efforts, time expenditure, and repetitive work by decreasing the workload on clinical staff, who can think innovatively for the good prognosis of patients [19].

ML models are built to perform the screening of various diseases to find molecules of pathogens [51]. Data is analyzed using various ML techniques and the performance of the algorithms are calculated with Area under the ROC Curve. Naïve Bayes (NB) gave the best results with AUC of 64% compared to other classifiers. Rules generated by J48 model was able to predict the disease symptoms which eventually help to take preventive actions and control measures to spread filariasis. ML algorithms are created based on public health and socioeconomic position data. This study took place based on the ML classification algorithms on dataset relevant to filariasis. T-statistic used for Feature subset selection. Gain ratio (GR) feature selection gave the best performance. This study enlightened the requirement of further research in this field to consider more features like immunological factors and climatic variables and to develop an incremental learning system based on new data in the dataset [20].

Romagnoni (2019) studied ML classification models to categorize individuals based on genomic data for Crohn Disease (CD), which is caused due to chronic inflammation in the gut. ML algorithms like LR, GBT and ANN on Immunochip data are used for this study. Non-linear algorithms performance is better in identifying and classifying genetic data than LR algorithms. ML algorithms conceded CD related loci with best values by using GWAS analysis. According to this study, DL algorithms proved to be most efficient and productive on unstructured data and GBM algorithm emerged as powerful method to predict CD [21].

B. Preliminaries:

Forlano et al. (2020) developed a software to measure fat, and inflammation levels, ballooning, collagen in liver diagnosis on Non Alcoholic Fatty liver Disease patients using ML techniques. Sourced data from 246 consecutive patients. Using ML algorithms Liver diagnostic report images are analyzed and compared the results with manual interpretation mechanisms. There is an exceptionally good similarity observed with manual interpretation mechanisms and ML algorithm generated reports. Results were very precise in finding if there are any changes in comparison with non-automated mechanisms. Binary LR algorithm used for generating variable to predict NASH presence. Liver diagnosis reports provide other useful parameters to treat any other ailments like too much of iron in NAFLD patients [12].

Le et al. (2020) developed an application using GBT algorithm-based models which have been trained on patient’s medical records to predict ARDS conditions at early stage. ARDS could be serious health hazard with excessive death rate and co-morbidities. Clinical variables and radiology reports data used in XGBoost library gradient boosted tree models of 9919 patients. As per the results that supervised ML algorithms can predict up to 48 hours before outbreak of ARDS in medical patients which will improve patient continuous monitoring, diagnosing, then providing treatment, and achieve good results [15].

Orange (2018) clarified microscopic anatomy scoring to diagnose RA sufferers’ tissue of synovial upon training the models with gene data using ML algorithms. RA disease occurs because of synovial tissue inflammation which will lead to the destruction of joints. SVM algorithm used to generate models with mRNA subtypes as labels, input as tissue structure data for the scoring. Patients who are suffering with high inflammation resulted in high levels of inflammation markers like C-reactive protein (CRP) and autoantibodies and patients with low inflammation levels has high level of neuronal and glycosylated protein mRNA expression, and pain’s level is not relevant to the higher-levels of chronic inflammation biomarkers. Data revealed that there are 3 different subtypes of synovial tissue, i.e., high inflammatory, low inflammatory and mixed subtype. This study was used with 45 synovial samples only, in future authors want to use larger dataset to get the better statistical results [22].

Panaretos (2018) tested accuracy of prediction on statistical and ML algorithm methodologies with respect to the relationship between food habits and cardiovascular disease risk. 3042 men and women are participated in this study. To calculate incidence of CVD, hypertension, diabetes mellitus the Item Response Theory (IRT) is applied. Factor analysis used to extract food habits and LR algorithm used to forecast their relationship with cardio metabolic results. KNN and RF machine learning algorithms used to assess the individual’s health who participated in the survey based on their food habits. ML techniques were useful especially linear regression in classification and best result-oriented techniques in health and nutritional field, which can be used to get higher accuracy levels to calculate the risk associated with CVD [26].

C. Considerations:

Villehuchet et al. (2009) described ML methodology to predict oxidative stress magnitude in humans. According to the studies, strong relationship exists between high levels of oxidative stress (OS), diminishing of the antioxidant protective mechanisms and the growth of various chronic illnesses like cancer, coronary diseases, and Alzheimer's. Biomarker profiles of OS measured to evaluate the probability and to predict OS levels quantity and antioxidant ranges. Range of subjects are included in diagnosis are like CVD (136), mental disorders (98), neurological disorders (61), arthritis diseases (34), communicable diseases (28), cancer (24) and endocrine system problems (20). During this study, NNs are used as in vectors and linear regressions. Authors inscribed the query of possibility of appropriate OS markers in relevant to chronic illnesses, and data pointed to 3 groups of markers: exogenous, endogenous, terminal markers. ML techniques are used to identify to forecast irregularities in markers of 1 group, especially in terminal markers, relative to marker irregularities in some other group. The possibility of forecasting markers of oxidative damage measured as part of this analysis successfully with ML algorithms [16].

Awaysheh (2016) tested supervised ML methodologies to comprehend between IBD & ALA diseases over cats. NB algorithms, classification tree models, and ANN models were used on blood work and blood chemistry tests result data. ML models attained higher precision like NB to 70.8% and ANN to 69.2% for classification process in comparison decision-based algorithm models. ML models enabled noninvasive tool as part of IBD & ALA diseases diagnosis to assist medical providers to comprehend between these 2 diseases, and between sick and healthy cats [23].

Cohen and Efroni (2019) proposed a system that provides variable inflammation reactions which preserve the human body and their complicity with collective genomes of the microbes while avoiding the menace from infectious substances. In this study 4 points are tested: 1). The body's defensive system can distinguish between good and bad cell states in body and body's defensive cells can convert from input signs to output of certain immunologic responses. 2). Individual body's defensive system cells groups respond together which is called crowd wisdom. 3). Cumulative inflammatory reactions are dynamic in action 4). Individual's autoantibodies and TCR collection in a healthy individual's body work in organic version based on experiential supervised ML which is analogous. This helps to monitor and treat autoimmune diseases, cancer, and allograft reactions. Even though the components of data are imperceptible to human eye, the interrelationships are perceptible by ML methodologies for example cell system and autoantibodies in body's defensive system. These interrelationships are used to interpret and test new data. Authors recommended that body's defensive system inflammation constitution is persuaded by datasets of training with autoantigen sensitivities [24].

Aravind (2020) used an advanced algorithm LIVERFASt™ to assess diagnostic precision of ML marker methodologies for liver detriment. NAFLD and resultant NASH diseases are widely spreading in the world. Generally, to diagnose NASH, an invasive liver biopsy is required. To identify NASH whether it is simple steatosis or advanced hepatic fibrosis is an issue in NAFLD patients. LIVERFASt™ tool created based on ML methodologies with 2862 biomarkers, in which 1027 biomarkers were used for training the model, 1835 consisted of validation dataset. 13,068 total cases considered for test and analyzed the reports to evaluate fatty liver disease. After the tests, 11% cases showed considerable fibrosis, and 7% cases had stern liver inflammatory symptoms, 63% cases had Steatosis and 20% had stern steatosis S3. SAF (Steatosis, Activity and Fibrosis) scores used in LIVERFASt™ algorithm to detect NAFLD (13.41%), NASH (1.08%) and advanced NASH (1.49%). LIVERFASt™ can be used to evaluate NAFLD and NASH to diagnose, to predict clinical path of individuals, and to provide of an efficient system for therapeutic interventions [25].

GBM based models can predict accurately on cancer related tumors characteristics. SVM is the only model gave unique output and can predict Patient's time of survival [27].

Dean and Hansen (2012) emphasize the importance of diet and active lifestyle in chronic conditions caused by inflammation and oxidative stress like in osteoarthritis. Healthy living can reduce inflammation and related pain to improve patient's health eventually reducing the need for medications and surgery [29].

Lötsch (2018) created a tool for diagnosing Multiple Sclerosis (MS) with unsupervised and supervised ML methods using non-invasive biomarker based on serum lipid omics and differentiate with other neurological disorders which may mimic MS [53]. This tool was able to forecast MS with the precision of around 95% [31].

IV. DISCUSSION

According to the literature survey, that Classification is the most important part of ML algorithms which is very much useful in medical systems to predict the stage of disease, and possible rate of survival of patient, which can further define the clinical course of action [27]. ML Algorithms used for classification: Logistic Regression, Decision Trees, KNNs, Naïve Bayes, SVM, Generalized linear models and RF [54].

DL used in prediction of disease, which is especially important in clinical environments, with good accuracy. Deep learning methods are extremely efficient on unstructured signal data. Random forest is best used in [21] microbiome research which is very crucial for gut health and diagnosing the underlying diseases [10], for classifying cytokine profiles which is essential to know inflammation levels and to generate whole blood gene information and informative gene modules [13]. RF classifier got classification veracity to 83% under cross-validation [14]. Multiple linear regression analysis is used in finding relationship between inflammation and diet [26]. Dietary habits play an especially important role on Gut microbiota which influences chronic inflammation [30]. Binary LR algorithm used to predict NASH disease by using markers like inflammation [12]. Decision tree-based methods best suited to SLE diagnostics [14]. XGBoost library implemented with gradient boosted tree models for prognosticating ARDS disease [15]. Neural networks are used as linear combinations. Support vector machine regression was used mostly in disease monitoring and management and to predict gene code subtypes, by using microscopic anatomy of biological tissues as input data [22]. Out of all classifiers Naïve Bayes (NB) gave the best results AUC of 64%. NB and ANN attained higher classification accuracy than the decision tree algorithm [20].

With the integration of ML methodologies and biological information would yield to higher opportunities to get accurate results in IBD investigation. This enhances the opportunity to fill the gaps between biological and computational data to generate valuable results for the greater benefit of individuals and to make the practices easy in medical industry. According to the author "interpretable machine learning models should be developed" [10]. If the sample size is exceedingly small Support Vector Machine is vulnerable to overfitting, thus the training data should be in sufficient quantity [17]. Poorly validated models can give bad results so comprehensive testing and investigations are essential along with practical validating methods to implement [10]. ML techniques use minimal computational effort, and easy to install, and calculate faster. Analyzing images and providing diagnostic facilities are done automatically without human intervention throughout the process is the biggest breakthrough with ML methodologies [12]. Selecting appropriate variables for the models can promote accurate results [16]. SVM and RF algorithms are favorites and used in creating the models for MS diagnosis [31], joint inflammatory diseases and IBD are commonly used in medical provision centers. RF algorithms can perform better than Decision trees methods. Due to overfitting K nearest neighbors lead to poor classification results. NNs and SVM can project with greater precision levels and these methods can extract features, but poor interpretability exists, and expanding to exceptionally large data is difficult. ML techniques must be evaluated for database limitations and potential learning errors before implementing them in clinical environments [19]. The choice of the feature is particularly important criteria in ML Techniques to diagnose and predict the diseases caused by inflammation [21]. Processes to learn, cleansing the data, preprocessing, feature engineering and selection are essential steps in ML modelling methodologies. Privacy is a concern for sensitive clinical data. Text-based medical records can be inaccurate unless expert human interventions included to review [17].

V. DATA ANALYSIS

Table 1. Machine Learning models test Accuracy with data sets.

Ref	*ML Algorithm*	*Accuracy*
[14] 2019	Random Forest Classifier	83%
[15] 2020	XGBoost Gradient Boosted Tree models	90%
[17] 2018	Support Vector Machine	88%
[18] 2020	k-Nearest Neighbors models	81%
[20] 2019	Naïve Bayes	61%
[20] 2019	K-means Algorithm	92.38%
[21] 2019	Gradient Boosting Trees	80%
[23] 2016	Naive Bayes and Artificial Neural Networks	70.8% and 69.2%
[26] 2018	KNN Algorithm and RF Algorithm	40% and 41%
[31] 2018	Clustering Algorithms	96%

VI. CONCLUSION

ML techniques are helpful to diagnose Inflammation biomarkers using algorithms like LR, RF, SVM and ANNs. There are 3 important factors to analyze to control inflammation. 1). Diagnosis of Inflammatory Biomarkers 2) To evaluate the disease symptoms and 3) Implementation of Diet and Lifestyle interventions. Analyzing individual inflammation Biomarkers and providing recommendations to follow certain diet and lifestyle changes could lead to autoimmune disease prognosis by avoiding deformity of the organs. Autoimmune disease symptoms can be reduced by controlling inflammation levels by following healthy diet and lifestyle interventions largely.

Machine Learning Algorithms play vital role to define personalized therapies based on individual's health conditions. ML Algorithms simplify the process of analyzing electronic medical records. Selecting the best attribute and larger data sets to evaluate a function is particularly important to get accurate results with ML algorithms. Most of the ML techniques are already used in medical industry for diagnosis and classification of the patients, still more research and technology usage is required to prevent the chronic diseases and autoimmune conditions which are impacted by inflammation before the individual turns into a patient.

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