ARTIFICIAL INTELLIGENCE IN RHEUMATOLOGY

Abstract

The recent advancements in information technology, has gained the interest towards the computer aided applications in medical field. Artificial intelligence is one of these technologies widely used in complex problem solving in scientific domain including medical research. AI facilitates the development of guidelines to create an evaluation model for autoimmune disorders based on the massive medical data. In the field of rheumatology, AI has a vital role in early diagnosis and clinical management of rheumatoid arthritis. RA is a chronic and remarkably heterogeneous disease characterized with the inflammation of synovial joints and it may lead to permanent bone damage. Hence, it is very important to detect the RA patients in early phase. This can be achieved by the various elements of AI including machine learning and deep learning. Therefore, AI tools facilitates the overall understanding of disease progression and aids in the early prediction of disease.

Keywords*:* Artificial intelligence, rheumatoid arthritis, Machine learning, deep learning, Inflammation, Autoimmune disorder.

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I. INTRODUCTION

This period of medicine id devoted to Non-Communicable Diseases (NCD)(Kumar et al.,2021).Rheumatoid arthritis (RA) is a non-lethalchronic systemic autoimmune disease that is associated with multiple bones and joints, and their adjacent tissues, such as wrist joints, fingers, metacarpophalangeal and metatarsophalangeal joints(Shaohui et al.,2021).(Yoo et al.,2017) described rheumatism as a pain in the locomotor system that declines the quality of life of patients. The global lifespan risk of rheumatoid diseases was 8.4 % for women and 5.1 % for men(Crowson et al.,2011).Yet, the exact cause of rheumatoid arthritis remain unclear genetic and environmental factors interact in a complex way and play a vital role in RA pathogenesis of the 291-illness examined globally, RA was the 42nd largest contributor to worldwide disability(Avramidis et al.,2022).The inflammation of the hands and wrists and morning stiffness are the major signs of Rheumatoid arthritis hence it still remains the cause of disability and deterioration of life for many patients (Mucke et.al.,2022). The progression of Rheumatoid Arthritis (RA) can be prevented by early diagnosis and treatment (Berend et al.,2019). Globally, one in 12 women and 1 in 20 men will prone to develop rheumatoid disease during their life span. (Crowson et al.,2011). Therefore, it is very important to diagnose RA patients in early phase for early cure(Yoo et al.,2017).

The diagnosis and prognosis for autoimmune disease like RAis highly unpredictable due to its heterogenicity (Stafford et al.,2020).The bone destruction seen in RA patients was totally irreversible. RA can be diagnosed using various imaging techniques like X ray, ultra sonography, MRI, and CT(Murakami et.al.,2018).However, these medical methods of RA diagnosis are quite expensive which cause an economical burden to aging population across the globe (Avramidis et al.,2022).Hence expensive therapies are still a major hurdle for many RA patients (Mucke et al.,2022).The symptoms of RA are almost identical to other diseases, hence it is very difficult to detect RA patients(Ali et al.,2018).In onset treatment of rheumatoid arthritis, a data-intensive investigation is required where artificialintelligence (AI) can play a crucial role in disease prediction(Imtiaz et al.,2022).

Previously, the aim of treating rheumatoid arthritis was to enhance symptoms, artificial intelligence (AI) has been used to perform this task (Berend et al.,2019). Although they are numerous biological and synthetic treatments for rheumatoid arthritis (RA)has been discovered, the decrease in the chronicity of disease is achieved only in a minority of patients. In order to overcome Man – made errors, computer-aided analysis is essential for an accurate and early diagnosis (Imtiaz et al.,2022).Recent studies have found that advances in ‘deep learning’ which is a sub field of artificial intelligence show better results than human observers in medical imaging analysis (Berend et al.,2019).The various applications of AI have been showing irreplaceable advantages in the field of rheumatology. Hence it is considered as boon to RA patients across the world (Shaohui et.al.,2021).Therefore, the quantification of early RA using these artificial intelligence tools has been the subject of research. (Berend et al.,2019).

II. RHEUMATOID ARTHRITIS

Arthritis is a degenerative disorder, characterized with different inflammatory conditions that show impact on various parts of the body such as joints, bones, and muscles. It is classified into various types such as Osteoarthritis (OA), Rheumatoid Arthritis

(RA), juvenile Arthritis, psoriatic arthritis, and gouty Arthritis. Rheumatoid Arthritis (RA) is an autoimmune inflammatory and a systemic disease which affect multiple organs(Imtiaz et al.,2022).Rheumatic disease is the most common disease in an aging population(Yoo et al.,2017).In recent studies it is predicted that about 15% of the Indian population are currently afflicted with RA (Suneetha et al.,2021).RA is considered as “multicausal” disease as it is influenced by a combination of genetic factors (human leukocyte antigen (HLA) encoding genes), environmental factors (smoking) and immune deregulations (generation of auto antibodies) (Khanna et al.,2019). Hence these factors affect the pathogenicity of the disease. (Imtiaz et al.,2022).

III. EPIDEMOLOGY

Joint space narrowing and Bone erosion are the most common characteristics observed in RA patients. Narrowing refers to contraction of cartilage between the bones which results in increased levels of pressure and friction whereas the Erosion is similar to bone resorption, in which the minerals release into the bloodstream due to breakdown of bone tissue. Even though it is part of a healthy life cycle of bone tissue, it is observed abnormally in patients suffering from rheumatoid arthritis leading to long-lasting damage (Maziarz et.al.,2022).It damages almost all synovial joints including the metacarpophalangeal (MCP), proximal interphalangeal (PIP), and wrist joints which results in pain and it is characterized with various symptoms such as awaking in the night and morning stiffness (Uretenet al.,2020). In addition, symptoms such as anaemia, dry syndrome, subcutaneous nodule are also observed (Yoo et al.,2017).In very few situations, lymph node enlargement is noticed mimicking Hodgkin’s disease (Avramidis et al.,2022). Globally rheumatoid arthritis is detected at the age between 30 to 60 in women and for men, it is noticed subsequently in various stages of life (Nkemdilim et al.,2018). Due to their behaviour during menstruation, pregnancy, delivery and breastfeeding which disrupts sex hormones and depletion of blood, women are three times more susceptible to RA than males (Shaohui et al.,2021).Even though there is no precise cure for RA, its treatment gives good results when it is diagnosed in early phase (Nkemdilim et al.,2018).

American College of Rheumatism (ACR) criteria of classification is used in the diagnosis of rheumatoid arthritis (Ali et al.,2018). ACR published a standard for the diagnosis of RA in 1987, but it was unsuitable for the early diagnosis of the disease. (Imtiaz et al.,2022). In 2007, European League Against Rheumatism (EULAR) was formed by a group of rheumatologists to create a new standard for easy prediction and treatment of RA disease (Kay et al.,2012). Recently in 2010, ACR/ EULAR developed a new criterion for detection and treatment of RA and to delay the disease progression and to enhance the chances of cure (Imtiaz et al.,2019). Erythrocyte sedimentation rate (ESR) and CRP and antibodies (such as RF and ACPA) are the common inflammatory markers that are associated with RA, which is the characteristic feature of autoimmunity (Khanna et al.,2019).

IV. TYPES OF RHEUMATOID ARTHRITIS

1. **Seropositive Rheumatoid Arthritis:** This is the most prevalent form affecting 60% - 80% of RA patients by triggering immune response to their joints as they shoe positive test for (RF), or (anti-CCPs), or (ACPAs) (Nkemdilim et al.,2018).

2. **Seronegative Rheumatoid Arthritis:** This category of patients will show symptoms to rheumatoid arthritis, yet they test negative to (RF), or (anti-CCPs) in their blood test (Nkemdilim et al.,2018).

3. **Juvenile Rheumatoid Arthritis:** It is mostly seen in patients of adolescent age (under 17 years) hence it is also known as Juvenile idiopathic arthritis. Most of the symptoms are similar to other forms of RA, in critical conditions eye inflammation and problems related to physical development are observed (Nkemdilim et al.,2018).

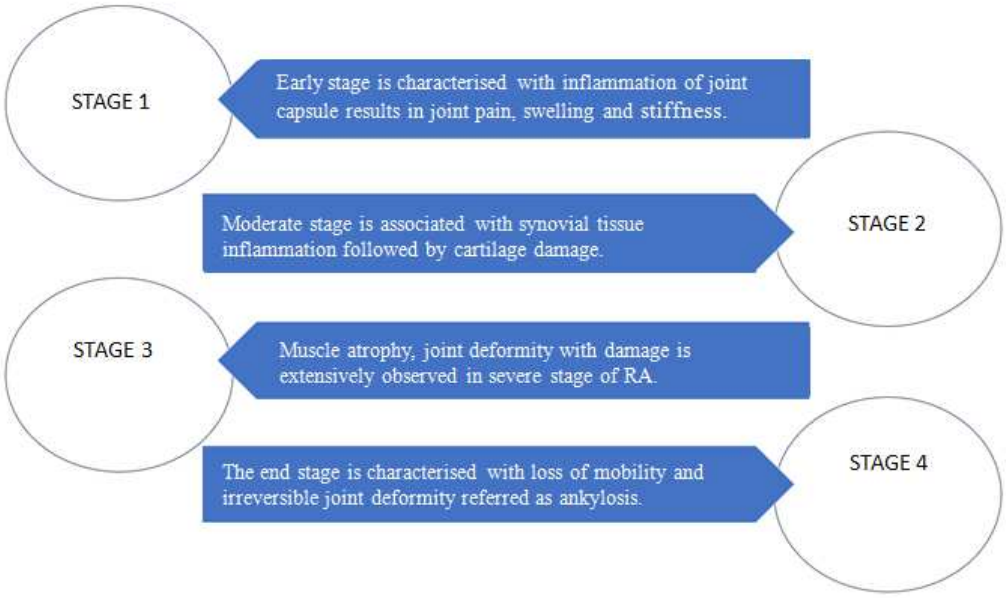

Figure 1: Visual representation of different stages of rheumatoid arthritis.

V. ARTIFICIAL INTELLIGENCE

Artificial intelligence (AI)is a branch of computer science that is capable to provide computers , the ability to solve problems intelligently and interact with humans by learning from them(Hugle et al.,2020).When a machine imitates the ‘cognitive’ functions of the human mind, such as learning and problem solving it is referred to as AI (Kothari et al.,2019)Human beings has sense organs, if they are imitated by AI to describe their surrounding environment it is referred as ‘Machine Perception’. If they imitate visual sense, it is referred as ‘Computer Vision’. From recent studies it is well-known that AI has become popular in almost every field. Hence, it is not new anymore(Steol et al.,2020).AI is used in our daily works including car driving, analysing a mammogram and it is also used in designing robots which mimics human behavior (Langlotz et al.,2019).

From the last four decades, AI is used to interpret medical images for diagnosis of pathological diseases, radiology, oncology, cardiovascular disease and to detect drug target in drug discovery, with steadily increasing success(Shaohui et al.,2021)Elements of AI had incorporated in the field of rheumatology which leads in the steady progress of success(Kothari et al.,2019). In recent era, AI is applied in various applications of medical world, especially in the treatment of RA(Shaohui et al.,2021).Artificial intelligence is used

for early and precise diagnosis and treatment of RA disease (Ali et al.,2018).Therefore, artificial intelligence is considered as the most profitable field across the world (Suneetha et al.,2021).

VI. MACHINE LEARNING

Machine learning (ML), is a subfield of artificial intelligence (Stafford et al.,2020).It has the capability to solve problems by using algorithmic methods and have the capability to interpret data automatically (Matsuo et al.,2022). Hence it is often referred as prominent field of AI (Obayya et al.,2022).Unlike the conventional statistics, these techniques are considered as most hypothesis-free as they complete their work by reconnecting the associations present within the data (Kim et al.,2019).Machine learning is no means new to world as it has been using globally, including Google's Alpha, TensorFlow, Microsoft Azure, IBM's Watson machine learning models like Deep Mind's and Alpha Go had proved that they can make complex decisions in real-world situations (Barberis et al.,2021). This may result in the huge discoveries, in the domain of artificial intelligence (Ghosh et al.,2022).

Machine learning has become a boon to various fields including medical research and IT (Yoo et al.,2017). Some ML algorithms uses patient's data collected from electronic gadgets like smart watch to check the health condition of patient (More et al.,2021). Machine learning techniques, are commonly used in diagnosis and treatment of disease and to detect biomarkers as well as to differentiate between healthy and diseased individuals thus proved to be more advantageous than traditional methods being simple and more precise (Barberis et al.,2022).

Supervised learning, Unsupervised learning and Reinforcement learning are the major subfields of machine learning (Hugle et al.,2020).

1. **Supervised Learning:** In this type of machine learning algorithm, it generates a relationship between input variables i.e., a set of instructions given by an expert (e.g., the rheumatologist) and output variables such as labels(Imtiaz et al.,2022). It is the prime approach used in the rheumatic studies (Jiang et al., 2021).

   Models are classified into two types: if they are instructed to output a choice of categories (e.g., low, moderate or active disease level) are called classification models, if they are instructed to output real numbers are called regression models (Hugle et al.,2020).

   Commonly used supervised machine learning methods:

   - **K-Nearest Neighbors:** The k-nearest neighbors are referred as a read-across model, as it predicts the outcome by utilizing only a few experimental observations of patients with unknown classification. Hence it is considered as lazy method as it categorises based up on the number of votes by k-closest training neighbours. (Barberis et al.,2022). It is applied for both classification and regression models (Imtiaz et al.,2022).

- **Support Vector Machine:** SVM is a binary classification algorithm that is applied for both classification or regression (Stafford et al.,2020).SVM uses hyper planes for classifying the input training samples into different categories. Hence it has the capability to assign newer samples into various categories (Imtiaz et al.,2022*).*
- **Decision Trees:** Decision tree is a highly competent supervised technique which provides a step-by-step decision-making process similar to a flowchart structure and each step is called as node, an attribute (e.g. rheumatoid factor (RF) is tested and they are categorised into various groups (RF positive and RF negative group)which will eventually decide the classification of group(Jiang et al.,2021).Therefore, the decision tree algorithm is sufficient for data sets consisting of different categories (Matsuo et al.,2022).
- **Random Forest:** Random forest is an advanced model than decision trees (Imtiaz et al.,2022).It uses bootstrap samples from the original data to create multiple decision trees(Lezczno et al.,2017).It is applied for both classification and regression models that has been adapted to predict the mortality rate of RA patients (Barberis et al.,2022).
- **Artificial Neural Networks:** Artificial neural networks (ANNs) are smart learning–based model composed of connected units referred as artificial neurons. They produce a theoretical representation of these that are organized as layers. The data flow from first layer (input) to the final layer (output) through a series of each intermediate layer called as "hidden layers"(Jiang et al.,2021). An ANN with numerous hidden layers considered as a deep neural network (DNN),it trains its own system from the information extracted from input data and produce a targeted output (Khanna et al.,2019).

2. **Unsupervised Learning:** Unsupervised learning does not require any class labels as it can predict the basic structure and pattern of data. Thus, the ML model with unlabelled data is referred as unsupervised learning (Imtiaz et.al.,2019).These are utilised for processing large medical databases, such as electronic medical records (EMRs) or large patient cohorts. This will help rheumatologists in better understanding of patient condition, to interpret the relationships present in the data and to focus their treatment on a particular disease characteristic (Hugle et al.,2020).

3. **Reinforcement Learning:** Reinforcement learning (RL) computers are intelligent based models as they are trained to act optimally in certain conditions(Hugle et al.,2020). It encourages the desired behaviours(positivevalues) by rewarding them and punish the undesired one(negative values)(Imtiaz et al.,2022). In rheumatology, RLplay a vital role in treatment strategies (Hugle et al.,2020).

VII. DEEP LEARNING

Deep learning(DL)a branch of ML, use artificial neural network (ANN) to automatically extract raw data, and to align this input data into desired outputs (Hugle et al.,2020).It consists of multiple layers of neurons where the first layer produces the input values while the last layer provides the classification. Deep learning will promote a new strategy where the whole image is classified in a single step. This approach helps in early prediction and diagnosis of RA (Berend et al.,2019).Deep Learning has huge impact on different fields in science(Maier et al.,2019).

VIII. CONVENTIONAL METHODS OF RA DIAGNOSIS

Recent studies have proved that the progression of rheumatoid arthritis (RA) is a multistep process and it is diagnosed by various steps and procedures that include physical examination, laboratory findings, and imaging findings(Zabotti et al.,2019).Even though RA is an incurable disease it can be treatment when diagnosed in early phase(Nkemdilim et al.,2018).Hence, it is very essential to detect rheumatic diseases in advance in order to improve the quality of life of an aging population (Yooetal.2017).

I. **Physical Examination:** In physical examination the clinician will ask about the patient's personal and family medical history. Tenderness, swelling, and painful or restricted movement are the major symptoms that are observed in physical examination. The physical examination may also reveal other characteristic features such as rheumatoid nodules or a low-grade fever (Nkemdilim et al.,2018). Because of these systemic symptoms it is very important to examine the whole body of RA patient along with the joints (Avramidis et al.,2018).

The Disease Activity Score (DAS) and DAS28 score utilizes the information from the tender and swollen joints to measure the disease activity of RA. The EULAR criteria categorise the RA patients as moderate and non-moderate responders based up on the chronicity and stage of disease achieved. The DAS28 is incorporated in several the electronic cohort records and web-aided systems are associated with DAS28 for regular clinical management and self-monitoring. This promotes "evidence guided practice" as it provides simple analysis of study results in clinical practice (Van et al.,2016).

Other popularly used score in the clinical practice of RA cohorts in CDAI (clinical disease activity included (Avramidis et al.,2022).

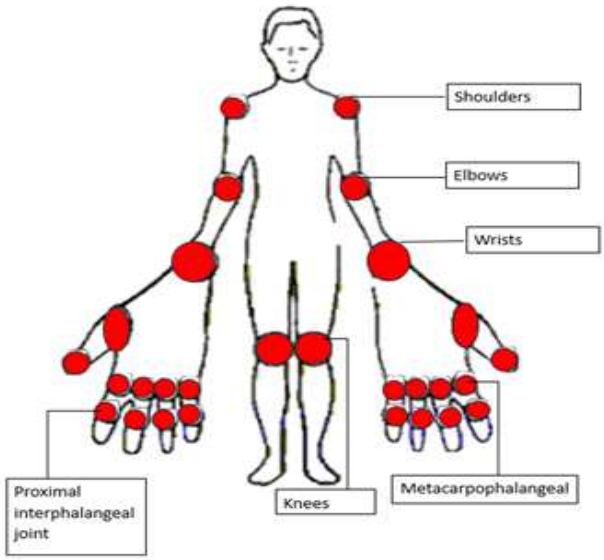

Figure 2: Disease activity score of 28 joints (DAS28) represents the chronicity of rheumatoid arthritis using clinical data.

IX. LABORATORY FINDINGS

The blood tests will screen for the presence of inflammatory biomarkers such as Erythrocyte sedimentation rate (ESR) and Creactive protein (CRP) and antibodies (blood proteins)levels present in the blood(Nkemdilim et al.,2018). In addition, they are screened for rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPAs) as they are the hallmark of inflammation. The presence of these biomarkers indicates that they seropositive RA but most of the patients show symptoms yet they show negative to blood test they categorized as seronegative rheumatoid arthritis (Avramidis et al.,2022).

X. IMAGE FINDINGS

Ultrasound (US), X-ray, computed tomography (CT) scans and magnetic- resonance imaging (MRI) scans are the popular medical imaging techniques used in the medical world. These imaging modalities are combined with the inflammatory symptoms and auto antibodies for early prediction of RA cohorts present in the advanced stage imaging methods like CT, MRI are used for screening multiple organs (Ker et al.,2017).

1. **Computed Tomography (CT):** Computed tomography (CT) is a slice imaging tool that facilitates the visualisation of 3D bone structure. It is capable to differentiate soft tissue and bone. Hence it is considered as gold standard model for identifying particular bone erosions. However, since CT use radiation for working, this may be one of the reasons for avoiding CT in early diagnosis of arthritis (Zabotti et al.,2019).

2. **Magnetic Resonance Imaging (MRI):**MRI is a non – invasive imaging modality used for prediction of bony erosions. From the last few decades, it is evident that MRI can identify twice number of erosions than sonography and radiography (Hoving et al.,2004).It has wider applications in the field of rheumatology(Khanna et al.,2019).MRI enables accurate evaluation of inflammation and structural damage observed in RA patients. It facilitates precise data on early symptoms of rheumatoid arthritis, specifically for predicting bone marrow edema and tenosynovitis. Globally, MRI plays a crucial role in diagnosis and treatment of RA patients (Zabotti et al.,2019).

3. **Ultrasonography (US):** Ultrasonography (US) is an accurate and non-invasive image modality and is capable of detecting swollen soft tissue and early bone lesions(Shin et al.,2020).In addition to MRI, sonography can detect extraarticular structures. When compared to MRI it shows more sensitivity towards tendon sheath inflammation of joints (Hoving et al.,2004). Sonography is sensitive to early phase synovitis and can identify more joint damage than radiography (Hoving et al.,2004).Therefore, this imaging tool is commonly used to measure disease activity of RA (Matsuo et al.,2022).

XI. NEED OF AI

It is evident that US economy use more than $ 80 billion annually in the clinical practices of rheumatoid diseases (Gescheider et al.,2022).It is hard to detect RA patients as they show shoe similar symptoms similar to other diseases(Ali et.al.,2018). The diagnosis and treatment of RA require expensive therapy and delay in diagnosis are the major hurdles faced by many RA patients (Mucke et al.,2022).Hence,the development of a computer aided system

is essential for quantitative estimation of RA in clinical management(Murakami et al.,2018).This computer-based system will certainly benefit RA patients by incorporating the data and interpreting it based on AI and medical big data (Shaohui et al.,2021).

XII. AI IN RA DIAGNOSIS

In the field of rheumatology AI and ML are widely used as promising approaches in early diagnosis, clinical decision making, prognosis evaluation and tailored treatment of heterogeneous disease such as rheumatoid arthritis. Medical big data, with digital data health technologies, such as artificial intelligence, machine learning techniques and deep neural networks, facilitate as an essential tool to incorporate such huge multidimensional data in a wide range of application fields, including patient diagnosis, identifying the patients at risk for autoimmune disease, classification of RA into different disease subsets, and to detect response to a specific therapy .Globally, there is a wide expansion of studies on artificial intelligence and machine learning models based on medical big data which are employed for easy diagnosis , early detection and avoid human errors unlike in conventional diagnostic procedures (Bartoloni et al.,2022).

1. **To Predict RA Patients:** Based on the clinical data of 60 anonymous rheumatoid arthritis patients provided by the Eulji University Hospital, (Yoo et al.,2017) suggested a study and predicted people with rheumatic disease by performing Clinical data analysis that regularly examined the threshold values of the rheumatoid factor, anti-CCP, SJC, and ESR variables used k-means clustering analysis to forecast that rheumatoid disease could develop if either RF or AC were positive. Rheumatoid factor > 7, anti CCP > 18, SJC > 4, and ESR > 25 were measured in patients with rheumatoid arthritis. Through the explanatory model, clarification evaluation values of 84% or more were attained.(More et al.,2019)documented that, by using thermal imaging and automatic segmentation, the abnormal part of the knee can be detected by employing C-means algorithm in 10 RA patient’s knee pictures.

   A Study reported by (Mate et al.,2019)on deep machine learning algorithms for diagnosis of diseases. It presented a method for detecting disorders like rheumatoid arthritis using various machine learning methods and artificial intelligence models. Accuracy of the joint localization active shape model was 96%. K-means picture segmentation demonstrated 93% accuracy rate, whereas counter delineation using ASM driven snakes reported 92% accuracy. (Kumar et al.,2021)describes a model that employs Machine Learning based Ensemble Analytic Approach (MLEAA) for early diagnosis of rheumatoid arthritis disease, it involves a detailed interpretation of ML algorithms associated with genetic components and clinical dataof RA patients. These precise parameters are employed to predict both affected and unaffected RA patients by using a voting approach. (Dulhare et al.,2023)developed a model for identifying and categorising rheumatoid nodules. Pure Deep Convolutional Networks (PDCNN) were used to detect rheumatoid nodules, followed by feature selection using Particle Swarm Optimization (PSO) and classification is performed by using the Residual Network (Res-Net). When compared to CNN and CNN with NCA, the proposed model shows better accuracy of 98.80% in feature extraction and classification. Therefore (Dulhare et al.,2023) concluded that this approach can widely applied in identification and categorization of rheumatoid nodules.

2. **Risk Prediction and Assessment:** A study of RA presented by (Vodencorevic et al.,2021) showed that, Twenty of the 41 patients evaluated had a total of 31 flares. The randomized-controlled RETRO trial's high-quality data are used to evaluate this machine learning study. This suggested that ML is an appropriate method to evaluate each patient's flare risk in RA patients tapering anti-rheumatic medication while achieving remission. This approach will aid in treatment tapering based decision-making and allow to achieve more precise in tapering and a consequent decrease in flare risk and treatment-related expenditures. Their team create astacking meta-classifier method produced an overall AUC of 0.81. Hence this ML-based prediction strategy may be able to target the right patients for treatment tapering and reduce the cost of expensive therapies.

   (Khanna et al., 2019) described Rheumatoid arthritis (RA) as a chronic, autoimmune condition that may increase the risk of stroke and cardiovascular (CV) events. Tissue characterization and risk stratification of RA is a complex problem. Low BMI promotes the systemic inflammation that causes serious cardiac events in RA patients. Recently, the Co morbidities in Rheumatoid Arthritis (COMORA) study found that 40.4% of RA patients had hypertension. It has been demonstrated that risk assessments using conventional ratings underestimate cardiovascular disease (CVD). Automated methods must be used to determine the CVD risk in RA patients because manual evaluation of the image-based characterization for carotid imaging results in significant intra- or inter-observer variability. Consequently, intelligence-based models such as machine learning–and deep learning–based techniques are crucial tools, and their automation offers a greater level of efficiency.

3. **To Detect Subtypes of RA:** (Orange et al.,2018) showed that the Krenn scoring system, which evaluates three histologic characteristics in synovial tissue stained with H&E but it did not distinguish between different rheumatic disease subtypes, such as RA and psoriatic arthritis. (Orange et al.,2018) and his colleagues proposed a more detailed histologic scoring system, that is used as a beneficial tool to subtype and direct the treatment of RA. In this study, we used the k-means clustering method to assess the relative usefulness of identifying 20 such markers for the separation of synovial subtypes. In order to learn more about synovial tissue inflammation and the sub classification of RA, we did an integrated study of clinical, histologic, and gene expression data from a cohort of 123 RA patients and 6 OA patients. Three synovial subtypes were determined by gene expression cluster analysis, and these labels were used to train a support vector machine (SVM) learning algorithm with scores of histologic features as the input. A histologic grading algorithm was created as a result of this investigation, and it may be used to forecast the three gene expression categories in RA and OA patients based solely on histologic characteristics. (Orange et al.,2018) came to the conclusion that the high inflammatory subtype is characterised by high synovial, systemic, and autoantibody levels. High neuronal and glycoprotein gene expression is a characteristic of the low inflammatory subgroup.

   (Obayya et al.,2019)developed an Arithmetic Optimization Algorithm with Deep Learning (ARAC-AOADL) model for Automated Rheumatoid Arthritis Classification. and employed this model to classify RA. They employed a multi-kernel extreme learning machine (MKELM) model for RA classification. In multi-kernel learning, the best linear integration coefficient and the classification parameter are learned equally using margin

maximization. An optimal kernel was regarded as linear integration of the group of base kernels. Two medical datasets are used to test the experimental result analysis of the ARAC-AOADL technique, and the results are examined from a variety of angles. The simulation results confirmed that the ARAC-AOADL technique had improved in terms of several measures.

4. **Targeted Therapy for RA:** Despite the fact that it has been well-documented that Tibetan medicine and other ethnic systems of medicine offer certain advantages in the detection and treatment of RA, there are still some practical issues, such as delayed detection, inappropriate treatment plans, and unclear medication mechanisms (Shaohui et al.,2021).With many similar treatment alternatives, it is difficult to determine which medication will work best for a given patient's disease cohort, and important time may be wasted by using various therapies that fail to help a patient attain their treatment goals(Gescheider et al.,2022).In rheumatoid arthritis (RA) patients, the top most targeted therapy is guided by synovial tissue transcriptomic and single cell analyses in prediction of targeted treatment response (Mucke et al.,2022).

   Currently, the important medications used to treat RA are divided into three groups: glucocorticoids (GCs), disease-modifying anti-rheumatic medicines (DMARDs), and nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs are typically used to treat severe joint pain and stiffness in RA patients. However, NSAIDs, such as aspirin and indomethacin, have a rather high prevalence of significant adverse effects in the digestive system. Artificial intelligence (AI)-based deep learning will provide accurate diagnosis and treatment of RA. Fromrecent studies it is evident that biologic DMARDs (b-DMARDs) and targeted synthetic DMARDs (ts-DMARDs), will bring a new era in the treatment of RA. In the early stages of an experiment or the creation of a new medication, supervised machine learning is recommended for screening and verifying potential target genes connected to RA illness. Worldwide pharmaceutical firms and pharmacologists are also showing a lot of interest in AI. An AI-driven biopharmaceutical company has unveiled a platform for the quick identification and validation of novel RA drug candidates as well as a deeper knowledge of the disease's biology. These developments may help to broaden the range of alternative RA treatment options that target new targets (Shaohui et al.,2021).

5. **Precision Medicine:** Recently, many publications have referred to the 5-20% of RA patients who are resistant to all existing treatments as "difficult to treat RA" patients. A personalized approach is the overall goal of the risk classification process (Sebastiani et al.,2022). (Mucke et al.,2022) emphasizes the critical requirement for precision medicine techniques to direct the treatment of RA patients. Due to their high clinical heterogeneity and significant variability in disease phenotype, development, and treatment response, systemic autoimmune disorders (Gescheider et al.,2022) make a suitable setting for the application of precision medicine models. There is a huge potential for machine learning in medicine, and uses predictive algorithms to bridge knowledge domains relating to patient features and projected medication qualities(Moingeon et al.,2023).Machine learning (ML) has rapidly emerged over the past ten years as a potential technology for producing personalized care (Mucke et al.,2022). (More et al.,2019)documented a method that uses neural network with real data from Saint's Raphael hospital to find appropriate

medications for rheumatoid arthritis. With a 97% accuracy rate, the recurrent neural network analyses data from LSTM and predicts the medications for RA patients.

(Gescheider et al.,2022) categorized RA patients as non responders and non-responders to anti-TNF medications, integrating Prism RA into clinical management of RA to improve the care of all RA patients receiving their first targeted therapy. As a result, Prism RA will prevent millions of dollars from being wasted on expensive drugs that aren't assisting patients in achieving their treatment goals. Regardless of the therapeutic field, this transformation is fuelled by big data and sophisticated computational analytics will hasten the discovery and development of more individualised medicines for the benefit of the patients.

6. **Predict Reemission in RA Patients**: At present, approximately 50% of patients with early RA reach sustained remission. Remission was defined as Erythrocyte Sedimentation Rate-based Disease Activity Score in 28 joints (DAS-28 ESR) of less than 2.6 (Vodencarevic et al.,2021).

(Koo et al.,2021) created a model using clinical information from the 1204 patient Korean College of Rheumatology Biologics and Targeted Therapy Registry. With explainable artificial intelligence, it is possible to forecast remissions in patients on biologic disease-modifying anti-rheumatic medicines (bDMARDs) and to pinpoint significant clinical traits linked to remission. In participants using bDMARDs, tumour necrosis factor (TNF) inhibitors, non-TNF inhibitors, and each bDMARD, remission was predicted using five machine learning models. Support vector machines utilising kernel techniques, tree-based random forests, and Xgboost were among the models. Based on the clinical characteristics of individuals with active RA, we effectively created machine learning models to predict remission as a response to several bDMARDs. Current effective therapies facilitate to attain remission even though few patients may experience relapse. A study developed by (Matsuo et al.,2022) attempts to predict relapse in RA patients using ML using data from US examination and blood test. The team use the RFE selection algorithm, or recursive feature elimination. There are three ML models used: Logistic Regression, Random Forest, and XGBoost. Additionally, we examined the results of eleven parameters (gender, illness duration, age, wrist SMI score, MTP SMI score, ESR (1 h), CRP, RF, anti-CCP, and MMP-3) that are frequently linked to disease activity and prognosis in RA patients. A potential strategy for practical and improved relapse prediction may include US examination, blood test, and ML model. The highest prediction was displayed by XGBoost among the three ML models with accuracy ofAUC =0.747.

7. **Image Processing:** In image recognition tasks, machine learning algorithms outperform humans, and it is expected that they will perform better in medical picture analysis as well (Ker et al.,2017). About 70% of all submitted papers at the 2018 International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI) dealt with deep learning (Maier et al.,2019). The emergence of large labelled data sets as a result of the digitalization of medical data has pushed the use of deep learning models in various medical imaging analyses(Avramidis et al.,2022). The resulting computer vision systems have the potential to revolutionize medical imaging, lowering diagnostic error rates, improve patient outcomes, increasing productivity, and lowering costs (Langlotz etal.,

2019). The four primary types of medical images are X-ray, ultrasound (US), computed tomography (CT), and magnetic resonance imagining (MRI) (Avramidis et al.,2022).

- **X-Ray:** X-rays are one of the most reliable methods for detecting ailments; deep learning was applied to make them more time-effective, which would help both doctors and patients. In order to identify whether or not a bone is healthy, an X-ray image of the bones is first used as the input data for a suitable supervised learning model. If it is discovered in the bone, the type of arthritis will then be determined whether it is Rheumatoid Arthritis or Osteoarthritis, by a Convolution Neural Network (CNN). Finally, the system will predict the severity of the bone damage, which is employed to take the necessary action (Suneetha et al.,2021).(Maziarz et al.,2022) demonstrated a multi-task deep learning model that can identify two types of joint damage—narrowing and erosion—while also learning to locate joints on X-ray pictures. The group suggests a deep multi-task neural architecture that uses the SvH approach to forecast joint narrowing and erosion scores. The team designed a deep CNN model to evaluate SvH scores for RA damage. Building models with SvH method will promote the interaction between machine learning models and medical professionals that facilitate RA diagnosis.

- **Ultrasound:** Using the OMERACT-EULAR Synovitis Scoring (OESS) system using DOPPLER US (DUS) pictures from RA patients, (Andersen et al.,2019) proposed a Two state-of-the-art method using conventional neural network (CNN) technology to categorise disease activity. Using a single neural network, pictures were classified as either unhealthy (Doppler OESS score 2 or higher) or healthy (Doppler OESS score 0 or 1). The maximum accuracy for the neural network assessing healthy/diseased score was 86.4% and 86.9% with a sensitivity of 0.864 and 0.875 and a specificity of 0.864 and 0.864, respectively. Their group findings imply that CNNs are capable of doing more intricate classification of DUS images.

- **MRI:** In 2007, one of the earliest attempts to measure inflammation in contrast enhanced MRI images of the hand was made by categorising the image intensities using ML (Fuzzy clustering) into normal and inflamed. As an alternative, synovitis has been measured using dynamic contrast enhanced (DCE-)MRI of the hand and wrist. The first traditional AI approaches used DCE-MRI of the wrist to measure bone marrow edema (BME). Numerous traditional AI techniques have been used to estimate cartilage thickness and volume in MRI data. BME could be determined automatically using static post contrast wrist MRI imaging, particularly in early RA. Deep learning is not yet capable to categorize MR images of synovitis. Classical AI techniques and deep learning are used in terms of MRI to identify bones as a preprocessing step for precisely characterising the synovium. Recently deep learning has widely used to detect and classify knee cartilage lesions (Stoel et al.,2020).

- **CT:** Traditional AI-based21 and CNN-based22 approaches were successful in identifying bone erosions using peripheral CT of the hand. By identifying pulmonary vessels that can be resolved by CT and then characterising their shape to provide imaging biomarkers, chest CT can be used to assess vasculopathy. These biomarkers provide an estimate of the number of small vessels and the ratio of small to large vessels (Stoel et al.,2020).

Table 1: Representative clinical studies of Rheumatoid arthritis using various AI models

AI Category	Model	Application	Reference
Supervised machine learning	k-means clustering	To predict RA patients	(Yoo et.al.,2017)
Machine learning	K-means picture segmentation	To diagnose RA	(Mate et.al.,2019)
Machine learning	(MLEAA)	For early diagnosis of RA	(Kumar et.al.,2021)
Deep learning	CNN	To classify rheumatoid nodules	(Dulhare et.al.,2023)
Machine learning	Stacking meta-classifier method	To predict patient's flare risk	(Vodencorevic et.al.,2021)
Machine learning	k-means clustering	To detect subtypes of RA	(Orange et.al.,2018)
Deep learning	(ARAC-AOADL) model	In classification of RA	(Obayya et.al.,2019)
Deep learning	Neural network	In Precision medicine	More et.al.,2019)
Machine learning	Support vector machine	To predict remission in RA patients	(Koo et.al.,2021)
Machine learning	XG Boost	To detect relapse	(Matsuo et.al.,2022)
Deep learning	CNN	To identify bone damage	(Suneetha et.al.,2021).
Deep learning	CNN	To locate joint damage: narrowing and erosion	(Maziarz et.al.,2022)
Deep learning	CNN	To categorize disease activity	(Andersen et.al.,2019)
Deep learning	AI-based21 and CNN-based22	To detect bone erosions	(Stoel et.al.,2020)

XIII. CHALLENGES

Despite of these advancements, there are still certain scientific issues that must be resolved despite this advancement (Imtiaz et al.,2022).

Due to patient privacy concerns and a number of other considerations, including ethical permissions, data scarcity is a severe problem in the field of medical research. There is currently no publicly accessible large-scale dataset for the training of data-hungry deep learning models (Imtiaz et al.,2022). Manual quality control of these massive volumes of data is therefore essential, otherwise, the neural network will train itself to produce errors that are identical to those made by people (Berend et al.,2019).The further difficulty in using machine learning to diagnose arthritis is data imbalance. Datasets that are currently available are unbalanced, and research papers do not address this issue (Imtiaz et al.,2022). A key barrier to the therapeutic application of AI algorithms is a lack of understanding of decision-making

process of trained deep learning algorithms. Therefore (Langlotz et.al.,2019), referred deep learning models as “black boxes”.

By overcoming these limitations, machine learning techniques will become more effective in translational medicine discovery and ambiguity reduction, enabling data-based decision-making to improve the next generation of diagnostics and therapeutics of RA patients at lower costs, and on a larger scale (Irure et al.,2022).

XIV. CONCLUSION

Early diagnosis of arthritis, including OA and RA, and to monitor the course of the condition is a challenging process. The advancements in digital health have created numerous opportunities for rheumatologists to maximize efficiency and improve patient outcomes. In the end, AI will serve as a tool in rheumatologists' toolbox to help clinical care and research. Once RA is identified, there is a window of opportunity to take control of the condition and prevent irreversible joint deterioration.

In 1997, the chief designer of Deep blue Feng-Hsiung Hsu that stated “we can use computers to extract knowledge from data, but human beings still have to turn that knowledge into wisdom” (Hsu et al.,1997). To sum up, AI can complement GP diagnostic intelligence but cannot completely replace it. We must make sure the AI-GP (general practise) combo improves diagnostic decision-making and health outcomes without merely making patients uncomfortable or placing an additional burden on healthcare finances.

REFERENCES

[1] Ali, A. H., Al-Ja'afari, M. A., & Abdulwahed, S. H. (2018). Rheumatoid Arthritis diagnosis based on intelligent system. *Journal of University of Babylon for Pure and Applied Sciences*, *26*(7), 47-53.

[2] Andersen, J. K. H., Pedersen, J. S., Laursen, M. S., Holtz, K., Grauslund, J., Savarimuthu, T. R., & Just, S. A. (2019). Neural networks for automatic scoring of arthritis disease activity on ultrasound images. *RMD open*, *5*(1), e000891.

[3] Avramidis, G. P., Avramidou, M. P., & Papakostas, G. A. (2021). Rheumatoid arthritis diagnosis: Deep learning vs. humane. *Applied Sciences*, *12*(1), 10.

[4] Barberis, E., Khoso, S., Sica, A., Falasca, M., Gennari, A., Dondero, F., ...& Manfredi, M. (2022). Precision medicine approaches with metabolomics and artificial intelligence. *International Journal of Molecular Sciences*, *23*(19), 11269.

[5] Bartoloni, E., Perricone, C., Cafaro, G., Alunno, A., & Gerli, R. (2022). The facts and fictions of precision medicine in autoimmune diseases: is the machine learning approach the response? *Rheumatology*, *61*(2), 484-485.

[6] Crowson, C. S., Matteson, E. L., Myasoedova, E., Michet, C. J., Ernste, F. C., Warrington, K. J., ... & Gabriel, S. E. (2011). The lifetime risk of adult-onset rheumatoid arthritis and other inflammatory autoimmune rheumatic diseases. *Arthritis & Rheumatism*, *63*(3), 633-639.

[7] DAS 28—Disease Activity Score Calculator for Rheumatoid Arthritis. Available online: http://www.4s-dawn.com/DAS28/(assessed on 25 July 2023)

[8] Dulhare, U. N., & Mubeen, A. (2023). Detection and Classification of Rheumatoid Nodule using Deep Learning Models. *Procedia Computer Science*, *218*, 2401-2410.Gescheider, A., & Saleh, A. Pioneering precision medicine in rheumatoid arthritis.

[9] Ghosh, S., & Dasgupta, R. (2022). Machine Learning and Life Sciences.In *Machine Learning in Biological Sciences: Updates and Future Prospects* (pp. 89-102). Singapore: Springer Nature Singapore.

[10] Hoving, J. L., Buchbinder, R., Hall, S., Lawler, G., Coombs, P., McNealy, S., ...& Connell, D. (2004). A comparison of magnetic resonance imaging, sonography, and radiography of the hand in patients with early rheumatoid arthritis. *The Journal of Rheumatology*, *31*(4), 663-675.

[11] Hsu, F. H. (1997). How the chess was won: An interview with Deep Blue's brains. *Technology Review*, *100*(6), 33-36.
[12] Hügle, M., Omoumi, P., van Laar, J. M., Boedecker, J., & Hügle, T. (2020). Applied machine learning and artificial intelligence in rheumatology. *Rheumatology advances in practice*, *4*(1), rkaa005.
[13] Imtiaz, M., Shah, S. A. A., &ur Rehman, Z. (2022). A review of arthritis diagnosis techniques in artificial intelligence era: Current trends and research challenges. *Neuroscience Informatics*, *2*(4), 100079.
[14] Irure-Ventura, J., & López-Hoyos, M. (2022). The past, present, and future in antinuclear antibodies (ANA). *Diagnostics*, *12*(3), 647.
[15] Jiang, M., Li, Y., Jiang, C., Zhao, L., Zhang, X., & Lipsky, P. E. (2021). Machine learning in rheumatic diseases. *Clinical Reviews in Allergy & Immunology*, *60*(1), 96-110.
[16] Kataria, S., & Ravindran, V. (2018). Digital health: a new dimension in rheumatology patient care. *Rheumatology international*, *38*(11), 1949-1957.
[17] Kay, J., & Upchurch, K. S. (2012). ACR/EULAR 2010 rheumatoid arthritis classification criteria. *Rheumatology*, *51*(suppl_6), vi5-vi9.
[18] Ker, J., Wang, L., Rao, J., & Lim, T. (2017). Deep learning applications in medical image analysis. *Ieee Access*, *6*, 9375-9389.
[19] Khanna, N. N., Jamthikar, A. D., Gupta, D., Piga, M., Saba, L., Carcassi, C., ...& Suri, J. S. (2019). Rheumatoid arthritis: atherosclerosis imaging and cardiovascular risk assessment using machine and deep learning–based tissue characterization. *Current atherosclerosis reports*, *21*, 1-14.
[20] Kim, K. J., & Tagkopoulos, I. (2019). Application of machine learning in rheumatic disease research. *The Korean journal of internal medicine*, *34*(4), 708.
[21] [22] Koo, B. S., Eun, S., Shin, K., Yoon, H., Hong, C., Kim, D. H., ...& Oh, J. S. (2021). Machine learning model for identifying important clinical features for predicting remission in patients with rheumatoid arthritis treated with biologics. *Arthritis Research & Therapy*, *23*(1), 1-10.
[22] Kothari, S., Gionfrida, L., Bharath, A. A., & Abraham, S. (2019). Artificial intelligence (AI) and rheumatology: a potential partnership. *Rheumatology*, *58*(11), 1894-1895.
[23] Kumar, S. S., Uma, R., Ramaraj, E., & Subhasri, P. (2021). Investigation on Data Mining and Machine Learning Techniques in Rheumatoid Arthritis Disease Research and Its Outcomes. In *International Conference on Mobile Computing and Sustainable Informatics: ICMCSI 2020* (pp. 753-763). Springer International Publishing.
[24] Langlotz, C. P., Allen, B., Erickson, B. J., Kalpathy-Cramer, J., Bigelow, K., Cook, T. S., ... & Kandarpa, K. (2019). A roadmap for foundational research on artificial intelligence in medical imaging: from the 2018 NIH/RSNA/ACR/The Academy Workshop. *Radiology*, *291*(3), 781-791.
[25] Lezcano-Valverde, J. M., Salazar, F., León, L., Toledano, E., Jover, J. A., Fernandez-Gutierrez, B., ...& Rodriguez-Rodriguez, L. (2017). Development and validation of a multivariate predictive model for rheumatoid arthritis mortality using a machine learning approach. *Scientific reports*, *7*(1), 10189.
[26] Maier, A., Syben, C., Lasser, T., & Riess, C. (2019). A gentle introduction to deep learning in medical image processing. *Zeitschrift für Medizinische Physik*, *29*(2), 86-101.
[27] Mate, G. S., Patil, M. S., Chavan, M. S., & Harshada, M. S. (2019). Automatic prediction of rheumatoid arthritis using CNN. *J Architect Technol*, 18-22.
[28] Matsuo, H., Kamada, M., Imamura, A., Shimizu, M., Inagaki, M., Tsuji, Y., ...& Fujii, Y. (2022). Machine learning-based prediction of relapse in rheumatoid arthritis patients using data on ultrasound examination and blood test. *Scientific Reports*, *12*(1), 7224.
[29] Maziarz, K., Krason, A., & Wojna, Z. (2021). Deep learning for rheumatoid arthritis: Joint detection and damage scoring in x-rays. *arXiv preprint arXiv:2104.13915*.
[30] Moingeon, P. (2023). Artificial intelligence-driven drug development against autoimmune diseases. *Trends in Pharmacological Sciences*.
[31] More, S., & Singla, J. (2019). Intelligent medical diagnostic systems for arthritis. *Int. J. Recent Technol. Eng*, *8*(2), 3626-3629.
[32] Mucke, J., Krusche, M., & Burmester, G. R. (2022). A broad look into the future of rheumatoid arthritis. *Therapeutic Advances in Musculoskeletal Disease*, *14*, 1759720X221076211.
[33] Murakami, S., Hatano, K., Tan, J., Kim, H., & Aoki, T. (2018). Automatic identification of bone erosions in rheumatoid arthritis from hand radiographs based on deep convolutional neural network. *Multimedia Tools and Applications*, *77*, 10921-10937.
[34] Nkemdilim, O. C. (2018). Differential diagnosis and tests of rheumatoid arthritis and its implication for physiotherapy. *International Journal of Innovative Research and Advanced Studies (IJIRAS)*, *5*(12), 18-22.

[35] Obayya, M., Alamgeer, M., S. Alzahrani, J., Alabdan, R., N. Al-Wesabi, F., Mohamed, A., & Alsaid Hassan, M. I. (2022). Artificial intelligence driven biomedical image classification for robust rheumatoid arthritis classification. *Biomedicines*, *10*(11), 2714.

[36] Orange, D. E., Agius, P., DiCarlo, E. F., Robine, N., Geiger, H., Szymonifka, J., ...& Donlin, L. T. (2018). Identification of three rheumatoid arthritis disease subtypes by machine learning integration of synovial histologic features and RNA sequencing data. *Arthritis & Rheumatology*, *70*(5), 690-701.

[37] Sebastiani, M., Vacchi, C., Manfredi, A., & Cassone, G. (2022). Personalized medicine and machine learning: A roadmap for the future. *Journal of Clinical Medicine*, *11*(14), 4110.

[38] Shin, Y., Yang, J., Lee, Y. H., & Kim, S. (2021). Artificial intelligence in musculoskeletal ultrasound imaging. *Ultrasonography*, *40*(1), 30.

[39] Stafford, I. S., Kellermann, M., Mossotto, E., Beattie, R. M., MacArthur, B. D., & Ennis, S. (2020). A systematic review of the applications of artificial intelligence and machine learning in autoimmune diseases. *NPJ digital medicine*, *3*(1), 30.

[40] Stoel, B. (2020). Use of artificial intelligence in imaging in rheumatology–current status and future perspectives. *RMD open*, *6*(1), e001063.

[41] Stoel, B. C. (2019, December). Artificial intelligence in detecting early RA.In *Seminars in arthritis and rheumatism* (Vol. 49, No. 3, pp. S25-S28). WB Saunders.

[42] Summerton, N., & Cansdale, M. (2019). Artificial intelligence and diagnosis in general practice. *British Journal of General Practice*, *69*(684), 324-325.

[43] Suneetha, J., Singh, P., Shrestha, K., Singh, A., & Bhagat, P. (2021). Arthritis Detection using AI. *Recent Trends in Information Technology and its Application*, *4*(3).

[44] Üreten, K., Erbay, H., & Maraş, H. H. (2020). Detection of rheumatoid arthritis from hand radiographs using a convolutional neural network. *Clinical rheumatology*, *39*, 969-974.

[45] Van Riel, P. L., & Renskers, L. (2016).The Disease Activity Score (DAS) and the Disease Activity Score using 28 joint counts (DAS28) in the management of rheumatoid arthritis. *Clin Exp Rheumatol*, *34*(5 Suppl 101), S40-S44.

[46] Vodencarevic, A., Tascilar, K., Hartmann, F., Reiser, M., Hueber, A. J., Haschka, J., ...& Simon, D. (2021). Advanced machine learning for predicting individual risk of flares in rheumatoid arthritis patients tapering biologic drugs. *Arthritis research & therapy*, *23*(1), 1-8.

[47] Wang, S., Hou, Y., Li, X., Meng, X., Zhang, Y., & Wang, X. (2021). Practical implementation of artificial intelligence-based deep learning and cloud computing on the application of traditional medicine and western medicine in the diagnosis and treatment of rheumatoid arthritis. *Frontiers in Pharmacology*, *12*, 765435.

[48] Yoo, J., Lim, M. K., Ihm, C., Choi, E. S., & Kang, M. S. (2017). A study on prediction of rheumatoid arthritis using machine learning. *International Journal of Applied Engineering Research*, *12*(20), 9858-9862.

[49] Zabotti, A., Finzel, S., Baraliakos, X., Aouad, K., Ziade, N., & Iagnocco, A. (2020). Imaging in the preclinical phases of rheumatoid arthritis. *Clin Exp Rheumatol*, *38*(3), 536-542.

