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ARTIFICIAL INTELLIGENCE IN PHARMACEUTICAL INDUSTRIES AND HEALTHCARE TECHNOLOGIES

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Abstract – *The complexity and rise of data in Pharmaceutical Industries and Healthcare Technologies emphasizes a great demand for* ***Artificial Intelligence (AI)*** *(see Glossary) in these areas. Artificial intelligence is not just one technology, rather a collection of them that focuses on improving accuracy and precision while performing any task. Our aim is to prepare a review article to understand and analyze the different approaches and applications of AI in the Pharmaceutical and Healthcare Domains. We have covered major aspects of AI under both these domains. Applications of AI in Pharmaceutical Industries explored in this review include use of* ***Clinical Decision Support System (CDSS)*** *(see Glossary) and Remote Patient Monitoring Systems (RPMS), Computed Tomography (CT),* ***Convolutional Neural Networks (CNN)*** *(see Glossary), Computational modelling for drug targets, Epidemic prediction and Random Forest (see Glossary) work on disease prevention. Applications of AI in Healthcare Technologies explored in this review include Genetic analysis, Virtual Nursing, detection of sepsis, Robotic surgery, drug discovery and precision medicine and cancer therapy.*

We have performed a detailed study and interpretations of all the points mentioned above in this review article. We have also done a comparative analysis highlighting the possible pros and cons of each application of AI in Pharmaceutical Industries and Healthcare technologies.

Key Words: Artificial Intelligence, Machine Learning, Deep learning, Neural Networks, Natural Language Processing.

1. INTRODUCTION

The galloping advancements in Biotechnology and Healthcare data are increasingly dependent on extensive use of Big data [29]. Artificial intelligence (AI) aims to mimic human cognitive functions thereby instilling a change in healthcare, due to an increasing demand [30]. AI uses algorithms to understand the parameters and characteristics from a large volume of healthcare data and then the information is used in assisting the clinical practice. AI forms two major categories **Machine Learning (ML)** and Natural Language Processing (NLP) where ML is used in analyzing structural data such as imaging, genetic and EP data while NLP is exploited to analyze unstructured data such as clinical notes. ML further gives rise to **Deep Learning (DL)** which uses artificial neural networks that can adapt and learn from an enormous amount of experimental data [31]. An AI system can be exploited to assist physicians by providing up-to-date medical information from various literature and clinical practices for proper patient care which can revolutionize the current reality of health care into the vision of continuous health care that promotes individuals in maintaining a constant health [32]. Also, an AI system can help in reducing errors from diagnostics and therapies. AI is being highly exploited in the medical field, ranging from digitization of medical records, to making a significant impact in robotic surgeries. It also finds mind-blowing applications in pharmaceutical industries ranging from drug development at small scale to the greatest extent of even epidemic prediction.

2. AI IN PHARMACEUTICAL INDUSTRIES

2.1 AI IN DRUG DISCOVERY, PROCESS AND DESIGN

The scientists are facing immense challenges in the view of developing an efficient and the most advanced systems in order to deliver the therapeutic agents onto the target with at most efficiency and least risks. Adding to it, in the development of new and novel therapeutic agents, its cost of development and the time taken for it is a great problem. So as to overcome this, AI and ML based computational modelling has become a new platform helping us to identify and validate the chemical compounds leading to the identification of the target. Determination of appropriate dosage of the drug using ML (see Glossary) and DL (see Glossary) algorithms has come up due to the emergence of AI.

- ML and AI are in wide use to identify and find novel targets and biomarkers associated with neurodegenerative diseases, to determine the potential genes with high risk of Alzheimer's Disease with the help of gene expression profiling.

- Computational methods are applied to study the protein-protein interaction, and protein-protein non-interactions and to predict the hindrance in PPIs.

- The ability to predict and estimate the overall dynamics of disease networks is one of the most significant outcomes of using algorithms of AI and

ML leading to the identification of novel molecular therapeutic targets for a specific disease.

Besides all these advantages, security-based issues are there which have to be tackled efficiently in the future. [17]

With an aim to reduce the cost and to decrease the immense time taken, AI or ML models can be used for outcome prediction of clinical trials which analyzes various factors in order to predict the probability of success. As an example, for predicting the outcome of phase I/II clinical trials, a DL based model trained using the score of pathway activation was utilized which could predict drug-induced pathway activation and the subsequent side effects. The goal being to support in silico clinical trials, these approaches could be developed by Virtual physiological humans. The physiological and pathological information regarding a patient at different locations can be synthesized with the help of AI or ML frameworks like these. [18]

In various fields of the discovery and development of the drug, AI has been used to recognize the hit and lead compounds, to quickly validate the drug target and to quickly optimize the design of the drug structure as well. Numerous in silico methods can be used for the virtual screening of compounds by eliminating the non-lead compounds at a faster rate and by selecting the drug molecules based on physiochemical and toxicological profiles with reduced expenditure.

Various tools centered on AI can be utilized for the prediction of physio-chemical properties. For example, ML is used to train a program and to optimize the performance of the compounds. Use of AI in drug design and discovery greatly reduces the enormous duration of time required in the process with decreased cost. [19]

2.2 AI IN DISEASE PREVENTION

Prevention of diseases is a good criterion to ensure proper sanitation and overall welfare. Supply of good drinking water is a global challenge for the governments across the world. A Bacterium named *Legionella pneumophila* is widely present in potable water and its colony forming units cannot be easily removed by the present disinfection techniques and protocols. This increases the risk for legionellosis, a deadly disease, causing chest pain and muscle weakness with pain, diarrhea, nausea or vomiting, fever or chills, coughing, mental confusion, etc. To reduce the occurrence of this disease among the public users, research was conducted to create a hot water tank simulator virtually with AI tools such as neuro-fuzzy systems, to prevent the disease. The major objective was to create a simulator of a virtual water tank in the aquatic environment which can instigate a situation that is widely common in water distribution in buildings. The notable characteristic of this model is its ability to adapt to any hot water tank. Upon considering the basic, vital parameters of hot water, a building maintainer and water supplier need to ensure the standard quality and temperature of water at every sampling site and prevent the spread of legionellosis. However, this model becomes successful with the use of quality samples and precisely trained neural networks [1]. This AI model must be extended further to be used in general environments. This is an essential criterion when we address public welfare. Besides, it can also be extended further to treat other water-borne pathogens apart from *Legionella pneumophila* which also pose a good threat to the people. If implemented, this AI model can become an essential component of water treatment plants which can treat water precisely and accurately without human intervened-errors. This model can also be used to predict the present conditions of the water to be treated and the treatment can be devised accordingly. This will reduce the possibility of overuse of water treating chemicals such as chlorine and other disinfectants and will in turn reduce biomagnification among the users.

Combination Therapy Development by employing AI can be a widely used strategy for infectious disease intervention. Project IDentif.AI aims at achieving this goal. IDentif.AI stands for Identifying Infectious Disease Combination Therapy with AI. This AI-driven project is used to analyze a parameter space of 12 drug/dose and rapidly identifies a possible combination therapy that can inhibit the A549 lung infection by a virus named vesicular stomatitis within 3 days after the commencement of the project. This project made use of the quadratic relationship between drug/dose inputs and efficacy/safety outputs to devise the optimal combinations of drugs to cure a disease [6]. This project was widely proposed to be used in COVID-19 therapies because COVID-19 creates a wide range of symptoms and chronic conditions in a wide variety of people suggesting a heterogenous manifestation of the disease. This is very essential to treat patients in a personalized way and devising a common therapy for diseases like this becomes a huge challenge. The project also guaranteed a seven-fold difference in the efficacy when compared to the other conventional combination therapies. Conventional combination therapies witness a manifestation of several diseases which develop as a result of side effects from treatments using a combination of drugs. Most of these side effects can be attributed to lack of time and knowledge to analyze and devise a personalized combination therapy for treating diseases. These types of AI projects can also provide a framework and base idea for other diseases for which treatment mainly utilizes steroids. The use of steroids has many benefits in treating diseases but it can also pose a lot of side effects in the form of immunocompromise to the patients, making them vulnerable to even more diseases in the near future. The spread of mucormycosis is also attributed to the overuse of corticosteroids in the treatment of diseases which can make the patients immunocompromised. These issues can be avoided by the use of these AI projects that can suggest a possible combination therapy according to the essential parameters characteristic to a given patient.

Postoperative pancreatic fistula (POPF) is a common cause of mortality worldwide after **pancreatoduodenectomy**

(PD) (see Glossary). It also delays the adjuvant delivery of therapies in addition to reducing the survival of the patients. This concern has also raised the need to select the patients who are potentially fit for PD and those who can tolerate POPF. This makes this therapy less accessible due to the aftermath effects of POPF. An AI model driven by ML was developed to estimate the risk of POPF in patients who have undergone PD. This risk prediction platform for POPF utilized two algorithms from machine learning, namely Random Forest (RF) and Neural Network (NN). The need for this AI model is increasing because the best way to treat POPF (a deadly pancreatic resection) is to prevent it. This AI-driven ML model also devised 16 risk factors for POPF and categorized them into 3 groups namely the technically demanding group, intraoperative volume status–related group, and poor general condition group [2]. However, there are several other risk factors that are not yet covered in these groups such as intraoperative loss of blood, transfusion, quantity of fluid administered, etc. These factors can also be taken into consideration while devising a possible procedure for PD. Also, there are correlations between alcohol use, physical trauma, cyst formation with pancreatitis which can lead to POPF. These factors should also be considered while developing an AI-driven algorithm for risk prediction of POPF. This AI model is a personalized therapy for patients who have undergone PD or possible treatments for pancreatitis. It also decides a personalized approach towards developing a post-surgery treatment to combat the effects of POFP.

2.3 AI IN DIAGNOSIS OF DISEASES

Artificial intelligence is widely used in diagnosis of several chronic diseases. The present-day problems witness a huge spike in the occurrence of chronic diseases and one of the major reasons attributed to the chronic nature of certain diseases is the inability to diagnose and detect them.

Colonoscopy is a widely used technique to detect colorectal neoplasia. Adenoma detection rate (ADR) is a useful parameter in colonoscopy and is used to estimate the risk of post-colonoscopy interval colorectal cancer. However, ADR alone is insufficient to spot and eradicate polyps once an adenoma is found. Therefore, another parameter called the adenomas per colonoscopy (APC) is also used. Several studies have shown the significance of sessile serrated lesions (SSLs) acting as notable precursors to colon cancer. Hence, advancements in colonoscopy aim towards improving the detection of SSLs to avoid the complications of colon cancer. Recent years witnessed the use of AI in improving the detection of polyps. An AI-aided tool also paved the way for improving ADR and APC for the detection of colon cancer. An AI-aided device named Skout makes use of deep neural networks to spot predominant polyps. It was also trained using videos of prospectively acquired full-length colonoscopy procedures. The study was performed with a large white population having high risk for adenomas. There was also a significant increase in ADR. To increase sensitivity and specificity by not detecting non-neoplastic polyps, the study also examined true histology rate (THR). This AI model was also effective in prompt identification of SSLs [3]. However, it is also important that this AI-aided polyp detection device should also be careful while diagnosing non-neoplastic polyps (harmless) in the colon which may be hyperplastic or inflammatory or hamartomatous.

Myocardial infarction (MI) is a deadly condition costing many lives worldwide each year. The current diagnostic techniques used for MI include Electrocardiography (ECG) and measuring cardiac troponins. However, the measurement of cardiac troponins requires special infrastructure, expertise in performing and is also time consuming. Employing deep learning strategies proves to be very useful in diagnosing arrhythmia, heart failure, left ventricular hypertrophy, valvular heart disease, MI, etc. Research was conducted to hypothesize an algorithm from deep learning to efficiently detect MI using 12- and 6- lead ECG. This algorithm works by identifying even subtle changes in ECG which can contribute to MI. The study used raw ECG data for the deep learning algorithm to extract features and for the prediction of cardiac arrest. However, several aspects need to be questioned before implementing this AI model into full swing. A retrospective study needs to be conducted to validate this model at home and general settings [4]. This is a highly crucial test because most of the effects of MI occur in an emergency setting and this model needs to be handy to reduce morbidity. There is also a necessity to check for independent decision-making characteristic of the developed model. The model also requires frequent updates in the form of new clinical presentations of the disease and efforts should also be taken to prevent it from getting outdated.

Diabetic retinopathy (DR) is a common consequence of long-term diabetes conditions and regular screening for DR must be a crucial routine for chronic diabetic patients. Sometimes, DR can also manifest in the form of Sight Threatening Diabetic Retinopathy (STDR). With a huge spike in the number of diabetic cases with early age of onset, it is very important to increase the awareness on screening for DR. The conventional screening techniques mainly include examination of fundus by ophthalmologists or retinal color photography through mydriatic or non-mydriatic fundus cameras. However, due to less sensitivity and specificity, there is a need for a better diagnostic approach which has been made possible with AI. AI has also integrated smartphone based retinal imaging, making this approach cost effective and more accessible. The study was based on patients with chronic type 2 diabetes to undergo retinal photography with Remidio 'Fundus On Phone (FOP)' which is a smart phone device driven by AI automation. The use of the EyeArt AI algorithm has obtained high sensitivity for the detection of DR and STDR. However, this model cannot be completely relied upon for those suffering from severe diabetic conditions and hence this puts forward the need for a consultation from an ophthalmologist to confirm the diagnosis despite the high sensitivity of this AI model. This research has also not utilized images from Remidio FOP to validate the EyeArt algorithm. It also poses greater challenges to obtain images for people with cataract and poor mydriasis. Thus, this smart phone-based AI-driven device will be highly helpful to persons with moderate diabetic conditions and these patients can track the severity of their diabetic condition from a home scale itself. Early diagnosis will be very helpful to prevent further damage to vision. In addition to these, a deep learning assisted AI model was also developed to diagnose and track other chronic eye conditions like age-related macular degeneration, etc. This study also emphasized the need of a proper evaluation from an ophthalmologist before proceeding onto further treatment or procedures [5].

2.4 AI IN EPIDEMIC PREDICTION

Artificial intelligence has emerged as a rapidly growing technological tool that finds its application in epidemic prediction.

Currently, the world is in the clutches of COVID-19 and history stands witness to a number of epidemics and therefore it is very important to immediately contain the pandemic. [24]

Artificial intelligence can be exploited to develop epidemic predictive models to prevent, control, and predict the spread of disease. [25]

Conventionally we use compartmental models that simplify mathematical modelling of disease that considers different epidemiological factors, mode of transmission, different class of population. Comparatively, AI driven epidemic predictive models are used as they show greater prediction efficacy and reliability.

Some AI driven algorithms are-

1) Evolutionary Algorithm- It includes:

a) Genetic Algorithm-

- These algorithms are a subset of computational methods and are based on the natural process of evolution that involves maintaining vital information in chromosome-like data structures using operators.
- Primary step involved is the generation of the population of chromosomes randomly, considering variables.
- These data structures generated called chromosomes are evaluated and those that display better solutions are taken to generate newer data sets. [25]

b) Particle Swan optimizer-

- Particle swan optimization is based on natural mass movement of birds in search of food. Each solution represents a bird in the group.
- Each element has a value based on the competency function and a velocity which remains constant at every step.
- Primary step involves establishing a well-defined population followed by evaluation and further analysis and updates in the velocity of particles.
- If the rules and conditions specified are not met then the cycle returns to initial steps [25]

These AI driven models play a major role in predicting the epidemic, thereby enabling control of the spread of disease with greater prediction reliability and efficacy.

2.5 AI IN REMOTE PATIENT MONITORING AND SUPPORT

Artificial intelligence in ICUs holds a great importance because it helps to detect the complications at an early stage and to detect the heightened risk of mortality. Monitoring the vital parameters of the patients is the main component of ICU. Its importance leads to the spread of patient monitoring across most of the sectors related to health. Although many people are confident and are viewing the current system of monitoring patients as a boon, the problems like increased rate of false alarms and involvement of sensor cables in numerous numbers have divided their opinions which has pushed for changes including sensors which are wireless, reduction in false alarms and requirement of hospital SOP for the purpose of managing alarms.

CDSS, which is based on AI could be used for predicting complications, detecting heightened risk of mortality, and proposing guidelines. With this system, the health data can be collected through sensors measuring vital signs from patients at one location and then transferring the data electronically to another location. At the next location, the specialists can then go through the data, access it and provide suggestions in order to manage the patients at the first location.

There are a few hurdles that have to be overcome in order to implement CDSS in the area of intensive care medicine.

- Technical infrastructure has to be established.
- Data science departments shall be developed by introducing novel CDSS tools by hospital providers ensuring effective use of AI. [13]

World over is seeing an increase in chronic disease which requires hospital treatment increasing their burden. Patient vital signs are extracted by invasive and non-invasive techniques and are shared with physicians in real-time which will enable doctors to take the right decision. There is a need for the development of an e-health system.

- In this e-health system, there will be continuous monitoring, prediction, diagnosis and treatment enabling the optimization of the health care costs.
- Patients can be monitored by doctors at anytime from anywhere. Thus, empowering them to be aware of their symptoms and treatments and helping them to have an independent life with better quality.
- PM systems are beneficial in ranking the patients as per their conditions, so that hospitals can prioritize critical patient care and also treat other patients in parallel.

Sensors which are wearable devices on the patient's body are part of a wireless body area network (WBAN) which will enable the doctors to monitor the patient's vital signs remotely. It holds an advantage of real-time recommendation using patient status by measuring vital signs remotely via wearable sensors, thus increasing the awareness of their status. [14]

With the help of risk-index on monitored symptoms, changes in patient's clinical status are checked and a National early warning score (NEWS-2) is given which is a good predictor of ICU admission. NEWS-2 which is a greatly efficient metric for monitoring COVID-19 patient's health status as the score is generated by NEWS-2 using the respiratory rate, saturation of oxygen, systolic blood pressure, consciousness level, heart rate, supplemental oxygen dependency and temperature of the patient. WHO has recognized the use of the NEWS-2 tool as it monitors the health of COVID-19 patients remotely and gives early warning scores. [15]

Real time measurements of signals from the patient's blood volume changes, urea kinetics, and thermal energy balance can be done by online monitoring systems containing automatic instantaneous bio feedback which helps in effective treatment. Anaemia is a serious complication in patients undergoing dialysis. Research has proved that the Anaemia control model (ACM) with artificial neural network (ANN) is used to estimate the future haemoglobin concentration. An algorithm is made to know the haemoglobin target by suggesting the optimal Erythropoiesis stimulating agents (ESA) and iron dosage. Ability of the data models to interpret is still a big challenge for decision making as research of AI on dialysis is at an early stage. [16]

3. AI IN HEALTHCARE TECHNOLOGIES

3.1 AI IN CANCER THERAPY

Cancer is listed as one of the common causes of high mortality worldwide costing millions of lives a year. A deadly feature of cancer referred to as metastasis holds a highly potential challenge in treating and curing cancer. Early detection of cancer metastasis is considered to be highly beneficial for devising a successful treatment and cure for cancer.

An AI model based on deep neural networks has been developed for diagnosing bone scintigraphy in cancer bone metastasis. Cancer bone metastasis is measured by a commonly used diagnostic technique called Bone Scintigraphy (BS). The major disadvantage with this technique is the high workload on physicians specialized in nuclear medicine. This AI model aimed to create an automated image interpretation system to aid diagnosis of cancer bone metastasis with improved sensitivity and accuracy. Although several imaging techniques have been developed, this AI model is regarded as a better alternative due to its high sensitivity and accuracy. AI models with the use of multi-input deep convolutional neural networks followed natural distribution, minimized judgments of physicians, enhanced performance and were closer to the usual clinical setting [7]. Examinations were done from 40 cancer types to diagnose cancer bone metastasis and the AI-driven bone scintigraphy proved to be effective. It was also able to detect small metastatic lesions that could otherwise be missed in conventional approaches. However, false positives and false negatives cannot be totally avoided and this model also requires approval by other confirmatory diagnostic tests to avoid further diagnostic errors. It would also be a wise idea to integrate other diagnostic tools such as CT, MRI and other cancer detection tests to have a complete analysis using this AI model. The use of deep neural networks in this model also serves as a greater advantage in the form of accurate decision making and interpretations from a multi-data input. This AI model can also be extended further to deduce the homing organs after metastasis and prior interventions can be taken to avoid organ damage. It can also be used for cellular level analysis for neoplastic cells and the data obtained can be used for designing selectable markers for antibody treatment to destroy cancer cells.

Breast cancer is a familiar type of cancer that contributes to a greater mortality rate among women across the globe. It is also listed as one among the most common origins for cancers of the brain, liver, bone, lung, etc. The conventional treatment for breast cancer mostly relies on radiation therapy but higher doses of radiation can also lead to cardiac failure and in the near future. An AI model was developed that assesses a DL system for volumetric segmentation of the heart on CT scans developed using cardiovascular radiology and is also used for the optimization of treatment plan in radiation oncology [8]. The model was developed and trained with the help of multi-center data comprising data from manual heart segmentations provided by the cardiovascular radiologists. To validate the model, a comparative study was performed on profiling the time needed to generate a clinically-validated segmentation without and with the assistance of a DL system. This estimated a significant reduction by 50% for the DL-aided approach compared to the present manual workflow [8].

This can in turn speed up the diagnostic process for heart illnesses and can also suggest a possible treatment to save lives. This model can also be extended further in risk prediction for infective endocarditis which is also called Subacute Bacterial Endocarditis when there is a history of rheumatic fever. This can lead to abnormalities in the heart valves and their associated structures and can slowly lead to severe complications associated with the heart and can prove to be fatal.

Metastatic Lung cancer patients are usually offered immunotherapy as a part of their treatment and immune checkpoint inhibitors offer promising results for the patients. An AI-driven deep learning model is used for monitoring lung cancer patients who are receiving immunotherapy as a part of their treatment. The model was developed on the basis of neural networks to identify and characterize morphological differences on CT reports during the patients' follow-ups by avoiding human intervention to the maximum extent (fully automatic manner). A classifier (Random Forest Classifier) was also incorporated to link the imaging features with the overall survival. This model also aims to analyze the possible prognostic value of AI-driven monitoring of CT scans in non-small cell lung cancer patients administered with anti-PD-1 immune checkpoint blockade [9]. The results from the model were also validated with the conventional clinical approaches by running a multivariate cox-hazards survival analysis [9]. This model can also be extended further to increase the sample space of patients receiving other immunotherapies. It can also be extended to small metastatic lung lesions that have the potential to trigger malignant tumors. It can also be extended to build a rough estimate of the homing organs that can be affected as a result of lung malignant tumors. It can also be developed further to do a molecular analysis of the cancer cells which can be used for the designing antibody therapies for complete cure of the cancer. It can also be used to predict the dormancy and relapse of the cancer which can become reactivated under favorable conditions in the future.

3.2. AI IN GENETIC ANALYSIS

For treating neurodegenerative diseases like Alzheimer's disease, AI can be used by analyzing genetics. With the help of this analysis, the fields of healthcare management and public health can be targeted. Binding affinities of functional consequences of noncoding variants, cis-regulatory elements, DNA and RNA binding proteins can be predicted by AI during research at gene level. Designing DNA probes for protein binding microarrays, generating protein-coding DNA sequences, and long non-coding DNA, analysis of exponential growth of genomic data and genomic modelling tasks can be identified and performed by AI.

AI technologies also predict disorder regions, protein contact maps, solvent accessible surface area, and secondary structure at protein level during research. There is still the challenge of prediction of tertiary protein structure. Data on genetic variations along with the risk of certain chronic diseases can be provided by genome-wide association studies (GWAS) along with thousands of single nucleotide polymorphisms (SNPs). [20]

Representations in the form of X -> Y, implying the occurrence of X suggests that Y occurs as well, is a part of Explainable AI (XAI). Representation of expression of several genes linked with expression of different genes is done by applying XAI to gene expression data (GED). Gene-specific TFs are one of the integral mechanisms which controls genetic changes in living organisms. Expression in the right cell at the correct time is ensured by regulating the turn ON and OFF of target genes with the help of binding of TFs to a particular DNA sequence. It is required to know the basis of gene interactions between TFs and their targets, so as to understand time-delayed relations of gene regulations in humans. Hence, it is proposed to have a database TRRUST including information that is relative to the relationships of transcriptional regulations between hundreds of genes. [21]

To forecast the impaired reaction condition for Huntington's disease (HD) patients, an assembly that combines several **artificial neural networks (ANN)** (see Glossary) of varied types to create a hybrid (neuro fuzzy) model is under research. Classification of accelerometer-aided tremor signals produced by Parkinson patient's involuntary movements can be done based on ANN like **multilayer perceptron (MLP)** (see Glossary). From the data of EMG sensors and triaxial accelerometers used by Parkinson patients, time-varying occurrences of dyskinesia and tremors are detected by using Dynamic neural network (DNN). Data taken from HD symptoms such as trembling in the legs, arms, hands impaired speech articulation and production issues are analyzed by making a prediction model design for Parkinson disease which uses decision trees and iterative Dichotomiser (UD3) protocols. For reproducing intelligent human reasoning processes, hybrid models are used which combine varied AI and ML approaches. [22]

Based on the input features from CADD but combined in a deep neural network which is a DL-based extension of CADD has demonstrated performance improvement. From the training data of 120,000 human samples, the network could learn significant protein domains, conserved amino acid positions and sequence dependencies. It is challenging to implement solutions through AI for the problems. Interpretation of complex data can be done by AI based algorithms which have superhuman abilities. Using AI solutions, may result in unethical and discriminatory results when applied on human health data. Definitely, for implementation of AI solutions, huge funds are required. [23]

3.3. AI IN VIRTUAL NURSING

Artificial intelligence is a powerful technique that can be exploited in the healthcare sector to resolve significant issues. Use of AI to revolutionize the healthcare industry for clinical decision support systems, has been extended to the diagnosis of various diseases like hepatitis and other forms of cancer. [28]

Machine learning driven experiments are proven to be more accurate, especially under the domains of pathology and imaging.[28]

AI technology now is partnered with nursing to complete tasks, rapidly synthesize information, assist in clinical decisions and improve patient outcomes.

AI-driven virtual nursing serves as a platform to provide personalized experience to patients. It enables patients to find the illness, chalk down the symptoms, monitor health status and schedule appointments as well. AI acts as an analytical system to serve as an optimal solution through thorough analysis of clinical data and existing data in literature.

One of the highly referred nurse avatars is "Molly". It is based on the use of a proprietary classification engine that allows it to listen and respond to the users.Another example includes nurse avatara "Angel". It checks the wellness of the patient through AI and voice for accurate diagnosis. It can communicate, manage monitors using unique insights and real time notifications.

These virtual nurses are available 24/7 and can process questions in real time. The application of AI in virtual nursing increases patient engagement and enables to improve self-management skills under severe conditions. These tools enable to avoid any chance of any missed diagnosis and enable real time diagnosis.

3.4 AI IN PREDICTION OF SEPSIS

Sepsis is one of the major causes of death and has affected a number of lives worldwide. It involves organ dysfunction due to a dysregulated response to infection. When chemicals are released in response to an infection, they trigger a severe immune response throughout the body that results in failure of multiple organs and can eventually cause septic shock. Hence, Early detection of sepsis is crucial.

AI driven SERA (Sepsis early risk assessment algorithm) algorithms are used to predict sepsis. It involves the use of unstructured clinical data as well as structured data in order to predict and diagnose sepsis. It consists of two algorithms- [26]

a) Diagnosis Algorithm- it determines if the patient has sepsis at the time of consultation or not. We use EMR system clinical notes for each consultation with the most recent structured variables available in the systems. [26]

b) Early prediction algorithm- the data structure is almost similar to the diagnosis algorithm but it doesn't take into account patient consultation via the samples obtained when the patient is diagnosed by sepsis. [29]

Machine learning is used to diagnose sepsis before its onset. Machine learning models used in the process are - left aligned model and right aligned model.

Left-aligned models predict the onset of sepsis at a definite point, point of consultation. Right-aligned models, also called real-time or continuous prediction models, continuously predict whether sepsis will occur after a specific time period or not. [27]

Hence, ML and AI driven algorithms have been exploited to develop sepsis prediction tools and can ensure early administration of antibiotics and pre-treatment before its predicted onset.

3.5 ROBOTIC SURGERIES

Modern-day people witness the emergence of highly complicated diseases and conditions. This puts forward the need for complex surgeries to save lives as well as reduce post-surgery trauma. This leads to a great demand for expert surgical skills as well as the need to maintain a sterile environment while performing the surgery. These criteria also led to the development of mechanized models to perform surgeries. Robotic surgery is regarded as the future of medicine to treat and cure diseases without human interventions and humanized errors.

A robot-driven system was designed for transforaminal percutaneous endoscopic lumbar surgeries. This system comprises three components namely preoperative planning system, navigation system, and foraminoplasty system. The preoperative planning system performs 3-Dimensional visualization of the surgical segment and the surrounding tissues and analyzes them using the multimodal image fusion technique of CT and MRI [10]. Care is also taken to decrease the risk of damage to crucial vessels and nerves. The navigation system obtains visual data from a visual receptor and automatically adjusts the robotic platform including the robot arm to the apt positions according to the patient's position and pre-operative plan. Intraoperative fluoroscopy is also used to register the surgical levels. The foraminoplasty system enables the robot to perform foraminoplasty using the high-speed burr at the end of the robot arm [10]. The prototype tests have been conducted and performance tests are also performed on simulations and cadavers to validate the system. The pre-operative planning system also suggests a 6 degree of freedom (DOF) robot arm employed in the navigation system. It has many advantages in the form of improving efficiency, accuracy and time consumption. It can get rid of multiple intraoperative fluoroscopies, reduce the exposure to contaminants due to the presence of surgeons and other medical authorities. It can also invite many new learners to come forward to handle such complex surgeries where even a small error can trigger fatal neurological disorders and disabilities [10]. This robot-aided system can also be further developed to be able to handle combinational surgeries and conditions. This can be achieved through complex AI algorithms. It can also be AI driven to be able to handle complications that can develop during surgery while keeping track of the anesthetic levels of the patients.

Robotic surgery also finds many applications to treat gastric cancer which is highly evolving. Robotic total gastrectomy with D2 lymphadenectomy along with a ''double-loop'' reconstruction method incorporated with intracorporeal robot sewn anastomosis (Parisi's technique) is a newly developed technique to treat gastric cancer [11]. It is a new strategy adopting a "double-loop" reconstruction method. This technique is widely developed in a need to promote "Minimally Invasive Surgeries (MIS)". This robot-assisted surgery takes place intracorporeally in one quadrant of the abdomen without any necessity to run multiple docking of the robotic system. This saves time as well as minimizes the instruments' movements [11]. The safety validation of this procedure was also confirmed with surgical failure analysis. The current focus also lies on investigating more advancements in MIS that can be incorporated in this robotic surgery. Expert training is also required to handle and operate the robot in a clinical setting. This robotic system can be further developed through AI driven algorithms using deep neural networks for carrying out combination therapies as well as reducing post-surgical trauma.

Urinary continence is a characteristic after-math of radical prostatectomy. Recent research aims towards developing a deep learning (DL) model to estimate urinary continence after **robot-assisted radical prostatectomy (RARP)** (see Glossary). Robotic surgical automated performance metrics (APMs) during RARPs, clinicopathological and clinical data from patients were collected from 100 contemporary RARPs [12]. The model also stratifies the expert guidance of eight surgeons and also validates the results using a historical cohort of RARPs. However, this model requires minimal human intervention and is likely to introduce bias when treating and operating patients with other comorbidities. Thus, it can be extended further through more complex AI algorithms to be able to decide on a combinational therapy and have a more personalized approach. Besides, it can also include the expert guidance of many more expert surgeons along with many conventional therapies. More historical cohorts of RARPs can be used to create a multi-data input that can be a good option to devise a more personalized therapy.

4. CONCLUSION AND FUTURE PERSPECTIVES

In this review article, we have analyzed the different approaches and applications of AI in the Pharmaceutical and Healthcare Domains. We have looked at various aspects of AI in drug discovery, disease prevention, disease diagnosis, epidemic prevention and remote patient monitoring systems under the pharmaceutical domain. We have also analyzed the role of AI in cancer therapy, genetic analysis, virtual nursing, prediction of septic shock and robotic surgery under the health care domain. We have discussed briefly on various algorithms used in these fields and its advantages and disadvantages. Although AI is exploited in various fields and are of great use during the COVID-19 pandemic as well, there are some shortcomings that need to be addressed. In the field of health care, for AI to perform as expected, it is to be extensively trained with curated data sets. But, because of issues related to privacy, it will be very difficult to get access to some data. In the future, we would like to perform different studies which would cover additional issues including those related to maintenance of privacy and protection. This review would help many researchers to acknowledge various facets of AI and the challenges associated with it.

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7. GLOSSARY

1. Artificial Intelligence (AI): artificial intelligence is the stimulation of computer systems to perform intellectual tasks
2. Artificial Neural Networks (ANN): computing systems inspired by Biological Neural Networks
3. Clinical Decision Support System (CDSS): Provides reminders to the health care providers so as to implement clinical based guidelines
4. Convolutional neural networks (CNN): deep learning algorithm which is used for taking an input image, assigning importance (weight and learning bias) to different aspects/objects of the image and being able to distinguish them from each other.
5. Deep Learning (DL): It is a part of AI and ML that mimics the same way as humans gain knowledge.
6. Machine Learning (ML): A type of AI which lets the software applications accurately predict the outcomes without being programmed to do so.
7. Multilayer perceptron (MLP): It is a class of feed forward artificial neural network consisting of a minimum three layers of nodes.
8. Pancreatoduodenectomy (PD): surgical procedure to remove cancerous tumours from the head of the pancreas.
9. Random forest Algorithm: It is a method for classification and regression which works by the construction of a multitude of decision trees.
10. Robot-assisted radical prostatectomy (RARP): Being a type of minimally invasive surgery, it uses surgical robotic equipment so as to remove the entire prostate.