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Systematic Review

Clinical Applications of Artificial Intelligence in Paediatric: A Systematic Review

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Abstract:

Introduction: Artificial Intelligence and Machine Learning have been the significant advancements of Science and Technology. Artificial intelligence (AI) a broad term that describes the use of machine-based learning algorithms and software, in healthcare settings. In diagnosing, treating and preventing diseases in paediatric population, AI could play a pivotal role. Paediatrics, a field that could have many practical challenges such as comorbidities, emergency admissions, and a lack of access to paediatric care providers, that could hinder quality and care provided to the patients. AI if implemented in paediatrics can streamline the work-force and help in clinical decision-making by making better use of clinician's knowledge and time. However various ethical concerns exist, regarding data privacy and safety. Instead of complete automation, it would be better to focus on collective human-support AI systems. Moreover, it is crucial that the explainability of AI models, potential opportunities, and challenges when integrating ML in healthcare, especially for the pediatric population, need to be evaluated. The present study is done with the aim of identifying role of AI in various domains in paediatrics. To analyse the ethical concerns in AI use in Paediatrics.

Objective: The study is planned to analyse the role of AI in various Paeidatric domains, to explore the potential benefits and limitations of AI integration into Paediatric healthcare systems.

Methods: A systematic analysis was carried out by analysing articles indexed in PubMed Central, Embase, SCOPUS journals in the English language. This methodical approach involved a comprehensive search, selection, and synthesis of relevant studies to address. The ethical concerns with its use, that are associated with AI use in paediatric population have been analysed.

Results: There is emerging literature on uses of Artificial intelligence in paediatrics. AI promises to improve accuracy, early diagnosis and treatment. The role of AI in paediatrics, the importance of various algorithms in diagnosing diseases such as neonatal jaundice, neonatal sepsis, traumatic brain injury, in various endocrine diseases and in malignancies have been analysed. The role of AI has shown promising results in early and non-invasive diagnosis in neonatal jaundice and neonatal sepsis, in classification of paediatric malignancies. However legal and ethical issues need to be addressed in more detail.

Keywords: Machine Learning, Paediatrics and Artificial Intelligence, Convolutional Neural Network, Algorithms.

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Introduction

The introduction of Artificial intelligence and Machine learning is the significant advancement of science and technology. The term artificial intelligence was first coined by John McCarthy in 1956, at Dartmouth conference.[1] Before coining this term, various names were used for Artificial intelligence as Cybernetics and Automata Theory.

The combination of computer science and statistics has enabled computers to learn, been regarded as a complex concept with considerable potential in medical care as well as in clinical research.[2] The tools such as ChatGPT (Chat Generative Pretrained Transformer),Bard and Glass AI 2.0 enables conversations amongst humans and machines. ChatGPT a Language Learning Model assists in healthcare, including helping patients with mental issues[3,4] Glass AI 2.0 helpful in generating differential diagnosis and clinical plan outputs.-The need of artificial intelligence is to lower the larger workforce need, and to enhance efficiency and work productivity in paediatric population. In previous decades, the use of Machine learning applications has drastically increased.

In paediatrics, the first computerised system was SHELP, used in the year 1984, for the diagnosis of inborn errors of metabolism.[6] Since 1984, ongoing research on ML in paediatrics has mainly focused on Deep Learning, Natural learning and regression analysis. The risks which are associated with AI could be untrained algorithms and racial segregation, thus patient care can be jeopardized.[7] In this review, we have analysed the role of AI in paediatrics, the importance of various algorithms in diagnosing diseases such as neonatal jaundice, neonatal sepsis, traumatic brain injury, in various endocrine diseases and in malignancies. The emphasis has been given to role of AI in paediatrics, with the help of qualitative approach to analyse data.

Terminologies used are:

Machine Learning: Artificial Intelligence's domain it is, that enables computers to learn from data and ML Algorithms are using various statistical techniques so that their performance can be enhanced and improved, with the use of various trained models. Machine learning could be supervised and unsupervised. In supervised ML(SML), the base is task driven regression, which mainly focuses on using the training data so that errors could be minimised. It is used as in distinguishing benign and malignant tumors. It includes labelled data training first, then validation set and finally generation of new dataset. Decision Trees (DTs): SML Algorithms and are easy to predict. In unsupervised/Unguided machine learning, the base focuses on data driven. In this data used is unlabelled and unstructured pattern recognition can be done It is used in Attention deficit Hyperactivity Disorder (ADHD), In which the researcher may use unsupervised techniques for the purpose of patients identification.

Deep Learning is a subfield of machine learning that includes deep neural networks(DNN) with many layers so that complex pattern can be recognised, it has gained success in recognition of images and speech.

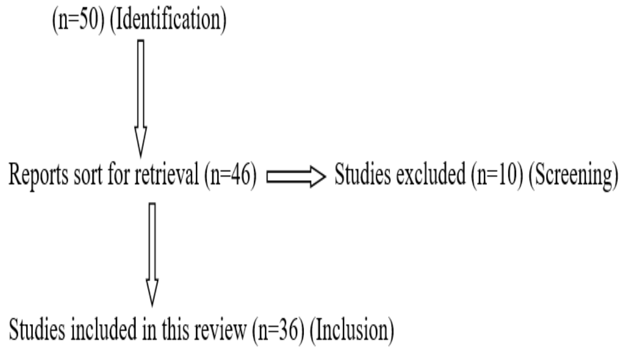
Natural Language Processing focuses mainly on interaction amongst human language and computers.

Large Language Models: These have high level of language understanding and language generation.

BARD: Building Auto reinforcement learning, can generate images as it has been powered with Geini, a new AI model.

PROMPT: Input text is given to the model and could have significant impact on the outcomes.

Material and Methods: In the following section of this review, we explore paediatric conditions, where AI-based approaches are being pioneered to support risk prediction, diagnosis, therapy. The present study is a systematic review and the protocol was registered in PROSPERO with code CRD42024604601. The database was searched with the string Machine learning and Respiratory distress syndrome, AI in paediatrics leukaemia, AI and medulloblastoma, AI and obesity, AI and Neonatal Sepsis, AI and Neonatal Jaundice diseases amongst children, AI and its cost effectiveness in Paediatrics. PRISMA (Preferred reporting items for systemic reviews and meta-analysis) guidelines were used for extracting data Records identified from datasets (n=50) (Identification)



Inclusion criteria: The original articles, systematic review that explore the AI application in paediatrics were included in this study. There were no restrictions regarding publication year.

Results

The articles covering Retinopathy of prematurity, Sepsis, Traumatic brain injury, Neonatal respiratory distress syndrome, Necrotising enterocolitis, Autism, Neonatal jaundice, Retinal Haemorrhage, Leukemia and Medulloblastoma have been searched and following mentioned studies have been included in this article.

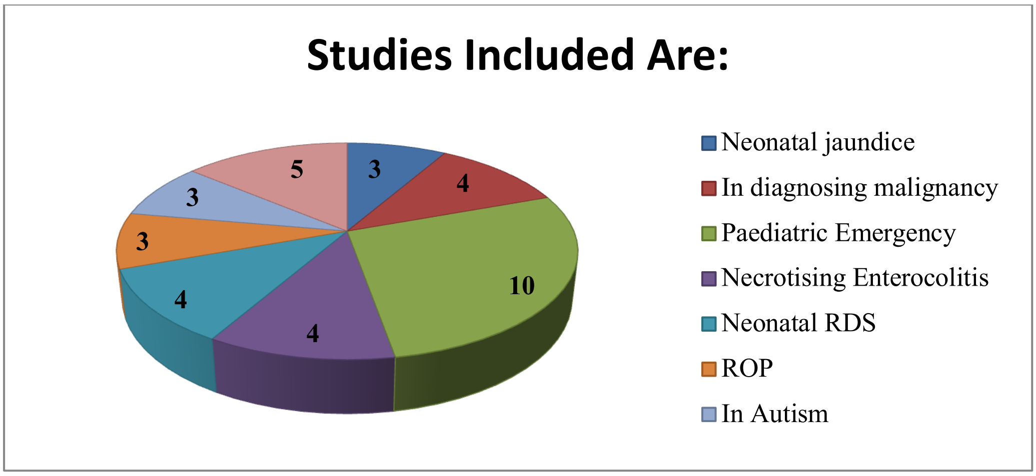


Figure 1: Number of Studies that are included in this review:

The Role and implications of artificial intelligence in diagnosing neonatal jaundice with various algorithms have been depicted in table 1. The studies included have shown high accuracy in diagnosis. The networks used in diagnosing malignancies, classifying medulloblastoma and assessing response of patients to treatment with the help of AI algorithms have been presented in table 2.

Table 1: Artificial intelligence in diagnosing neonatal jaundice:

Study	Algorithm/Model	Results
In a study by Aydin et al, in detecting neonatal jaundice.	KNN (K-nearest neighbour and support vector regression algorithm) was used.	The model has detected jaundice in 40 patients with the help of images. And the success rate was 85%.[9]
In a review by Salami FO et al.[10], 33 articles that have satisfied the research criteria were included.	The study has analysed the noninvasive techniques of diagnosing neonatal jaundice by capturing neonatal images. These images can be analysed using AI based technologies. The most commonly used tools are Optical Spectroscopy, Smartphones and Reflectance Photometers.	Deep learning model has shown outperformance in contrast to Machine Learning model.
In a study by Makhloughi F et al, 2235 images of 745 infants were included. [11]	1 DCNN using conventional layers, max pooling layers and dense layers was used to analyse neonatal images and to predict estimated bilirubin levels.	The accuracy was 96.87%, outperforming machine learning and deep learning models. The squared R value was 0.9, which indicates that model captures bilirubin estimation effectively.

Footnote: "KNN-K-nearest neighbour,; SVR: Support vector regression;1DCNN:1-dimensional convolutional neural network**,** Squared R value indicates proportion of variance in bilirubin levels explained by model.''

Jaundice is the yellowish discolouration of the skin, mucous membranes and sclera, caused by hyperbilirubinemia. The invasive painful method of measuring TSB has been replaced by using non-invasive methods in AI such as transcutaneous bilirubinometer, optical spectroscopy and reflective spectroscopy.

Table 2: Role of AI in diagnosing Malignancy in paediatrics:

In a study by Pan L et al, which is aimed at identifying prognostic factors that are related to relapse. To predict intensive treatment need in cases of relapse.	486 children, who have achieved complete remission after induction therapy were included. 121 children have relapsed after completing first remission. In early detection of relapse, Random Forest (RF) and Decision Tree (DT) were superior to Logistic Regression (LR) and Support Vector Machine (SVM) in the present study.	These models were designed on the basis of gene expression data or combined MRD and IKZF1 (Ikaros zinc finger-1 gene status), these have achieved accuracy ranging from 0.735 to 0.790. [13]

In another study by Huang F et al, 380 images from healthy subjects, 400 from AML and 302 from ALL patients,240 from CML patients were included.	GoogleNet 22 Layer,—ResNet and DenseNet-21 (3 CNN frameworks) have been used to construct classification.	The results of DenseNet-121 were better in bone marrow cell microscopy images classification.[14] This approach has resulted in accuracy of >98% in detecting both types of leukaemia.
In a study by Attalah O et al, paediatric medulloblastoma images of <15 years of age were included. [15] With the use of three CNN(ResNet-101, Inception and InceptionResNet) and texture analysis, the analysis of 154 medical images were done. For classification of Medulloblastoma, both histological and textural images were used. Six classifiers used, have resulted in accuracy of 98.34%(LDA),98.7%(QDA),97.04%(SVM),98.7%(NB), 98.1% (kapaa NN), 96.7% (RF). the classification accuracy of medulloblastoam could be 100% by combining information from textural images with the original histopathological images. The dataset consisted of pediatric MB tumor images for children of age <15 years [15] Three CNNs ResNet-101, Inception, and Inception Res Net models were used. Six different classifiers (LDA, QDA, SVM, NB, KNN, and RF classifiers) with three CNN architectures (ResNet-101, Inception, and InceptionResNet) were used. The classification accuracies for the six classifiers that are trained with the fused deep textural features were higher.		
In a review by Chen ZJ et al, results of AI were satisfactory, has included 1081 cases of <10 years of age[16]	With the use of GLCM (Gray Level Co-occurance Matrix)	AUC was 0.87 in analysing cell morphology.

Footnote: RF:Random Forest; DT:Decisiom Tree; LR:Logistic Regressin; SVM:Support Vector Machine; CNN:Convolutional Neural Network; LDA:Linear Discriminant Analysis; QDA:Quadratic Discriminant Analysis; NB:Naive Bayes; KNN:K-nearest neighbours; GLCM:Grey Level Co-occurence Matrix; AUC:Area under the curve.''

Leukemia: A hematopoietic malignancy and its incidence was ranked 15th among all malignant tumors, and its mortality rate ranked 10th.[12] For the purpose of initiating correct and early treatment, the disease classification is a prerequisite. Another important model used in paediatrics is Convolutional Neural Network (CNN), a perceptron model. The main strength of CNNs lies in its ability to automatically extract features from an image. These networks carry a great capacity to analyse and employ images directly for diagnosis and it eliminates the excessive processing steps that are usually required conventional machine learning techniques. The three main layers of CNNs are the convolutional, pooling, and fully connected (FC) layers. Within the convolutional layers, convolution carried out between image segments and a filter of small size. Following that, a feature map containing the spatial information of the pixels in each segment of an image, is produced. The pooling layer then diminishes the huge dimension of such features by downsampling.[12]

AI in Paediatric emergencies:

a) In Traumatic Brain Injury (TBI): A very common and serious complication amongst premature infants. In identifying whether a child needs CT scan or not, Paediatric Emergency Care Applied Research Network (PECARN) is used, but to improve the treatment care with the purpose of starting it early, deep artificial neural network used in a study by Ellethy H et al, has resulted in 98.6% sensitivity and 99.7% specificity.[17]

Another model for detection of TBI, 2 way 11 layer deep CNN, in which resting state functional network connectivity have been used in detection of TBI.[18] The results were being favourable in ANN algorithm. On the contrary, Gravesteing et al, has concluded that ML doesn't outperform than traditional logistic regression in TBI.[19]

b) In Sepsis: In children sepsis is defined as the presence of systemic inflammatory response syndrome (SIRS) in the setting of known or suspected infection. The diagnosis is usually made on clinical symptoms and signs accompanied by bacteremia. This still contributes to mortality and morbidity in neonatal intensive care units (NICUs) as well as low- and middle-income countries The initiation of specific treatment is delayed as blood culture reports may take several days. Clinical algorithms used for initiation of therapy are maternal: urinary tract and sexually transmitted infections, premature rupture of membranes, intrapartum fever, chorioamnionitis, and/or malodorous discharge, and neonatal risk factors such as prematurity and low birthweight), as well as neonatal signs and symptoms including (temperature >37.7 or >35.5°C, bradycardia, respiratory rate > 20/min or hypotension, tachycardia, apnea, hemodynamic instability, and abnormal laboratory data: white blood cell counts > 12,000/mm3 or < 4,000/mm3). Therefore, the development of new neonatal sepsis diagnostic tools that could consider individual combinations of clinical variables can be used as a tool to reduce the time taken to initiate antimicrobial therapy. [20]

In the present study, we have gone through the datasets, to analyse the sensitivity, specificity and types of AI models used in early detection of neonatal sepsis (Table 3)

Table 3: Models analysed for NEONATAL Sepsis:

Models used	Results
RF based ML Algorithm	For the purpose of prediction of septic shock has shown specificity of 98% and sensitivity of 26%.[21]
ML Algorithm for up to 48-hour advance prediction of sepsis using six vital signs [22]	For predicting sepsis onset at least 48 hours prior. Machine learning model has depicted high sensitivity and specificity in predicting sepsis.
Explained AI model (XG Boost with Bayesian optimisation)	Has shown sensitivity 90%, specificity 64% .[23]
Deep learning model on electronic health records for early detection of sepsis	The present study proposes a new retrospective evaluation technique to assess the clinical utility of the model, for both intravenous antibiotics and blood culture requisitions. The evaluation has shown at the time of early detection that a large proportion of sepsis patients had not initiated intravenous antibiotics or blood culture and thus the model could facilitate such interventions at an earlier point in time. [24]
ANN consisted of 25 maternal and neonatal features connected through coefficients to a hidden layer, output layer, for early detection of neonatal sepsis. Diagnosis of sepsis is coded as one and non-sepsis as zero.	The model sensitivity is 93.33%, and positive predictive value is 82,35%.[25]

Footnote: "RF:Random forest, ML:Machine learning; XG Boost:Exttreme Gradient Boosting; ANN:Artificial Neural Network; EHR:Electronic Health Record.''

Methods or algorithms used for early detection of neonatal sepsis, are random forest (RF), logistic regression (LR), Neural networks (NNs) and XG Boost which can span from statistics that is basic to AI models that are complex, as are analysed in table 3. The success in antimicrobial therapy for neonatal sepsis depends on early detection and knowledge of sepsis epidemiology inside neonatal intensive care unit. [26]

AI in Necrotising Enterocolitis(NE): In premature infants, interstitial peritonitis (IP) could be necrotising enterocolitis and spontaneous interstitial peritonitis (SIP). [27] NE is a devastating complication amongst premature infants. The presence of signs(nonspecific), such as apnoea with decrease in heart rate and fall in oxygen saturation, vomiting, abdominal discomfort are usually considered in making diagnosis, although this results in low predictive value. Many of the clinically diagnosed cases usually do not meet the typical radiological features of Bell's staging criteria.[28] The progress of AI in Neonatal interstitial peritonitis is lacking, but ML techniques have been used for individualised NEC risk scores.[29]

AI and Neonatal respiratory distress syndrome: RDS commonly affects premature infants: The use of less invasive surfactant in premature infants can reduce the need of mechanical ventilation, in neonatal respiratory distress. ML models have been introduced for the early diagnosis of RDS. In one study, in a multivariate regression model using perinatal factors: the area under operating characteristic curve(AUROC) was 0.760, thus the accuracy in diagnosing NRDS was low.[30] However in another study, support vector machine (SVM), RF and ANN, AURO was 0.97to 100, but inconclusive results due to small sample size.[31]

In another study Korean Neonatal Network, on large dataset, was used for enrolment of very low birth weight infants (VLBWIs) <1500gms. Various Machine learning models such as Gradient boosting machine, extreme gradient boost, adaptive boost, Light gradient boosting machine, were compared. To improve the prediction performance, 5 layer deep neuronal network (DNN) was selected and it has shown sensitivity 0.8360 and specificity of 0.8563 with accuracy of 0.8407. [32,33] At the end, on the basis of top 20 factors from VLBWIs, a public web application was developed for prediction of RDS. Therefore, enables the more smooth resuscitation in neonates. This app does not store any information, so protection of personal data.

Role of AI in Retinopathy of Prematurity (ROP): In premature infants, retinal vascular growth is delayed and abnormal blood vessels are formed. In diagnosing ROP plus diseases, inter observer variation is high, thus ROP detection and starting its treatment earlier is crucial. ROP can lead to infant blindness and most important to note is that annually 3.5 million babies born in india are premature weighing <2000gms. And if ROP is diagnosed early, it is a treatable condition.[34] It is one of the most common etiology of blindness amongst children. In this review we have analysed the datasets predicting the importance of models for early diagnosis of ROP.

In a study by Rao DP et al, tele ROP programme has covered 30 districts in south india, in a period of 2011 to 2022. In this, with the use of 130 degree lens , six fundus images including macula densa, temporal, superior, nasal and inferior quadrants, disc centre per infant were collected. Thereafter, for the filteration of images, an assistive neural network (CNN) was used. This has resulted in overall specificity of 91.22% and sensitivity of 91.46%, in diagnosing ROP. [34]

In another study by Liu Y et al, two deep learning models DenseNet-121, ResNet-18 were used and the data was collected from 651 preterm infants with mean birth weight 1546.3+/709.5gms, DenseNet-121 has shown better performance in ROP screening and ResNet-18 has performed better in deciding which treatment option to adopt for ROP. [35]

The AI system has been used for Task 1: which identifies whether the preterm has ROP or not, for Task 2: To predict whether ROP patients need treatment and for Task 3: To suggest treatment options for preterms suffering from ROP. The analysis of retinal images with retinal cameras has improved ROP evaluation efficacy.

AI in Endocrine diseases:

In Paediatric Diabetes: In a single centred, observational, single arm study type 1 diabetics of <18 years of age who use continuous glucose monitoring, were included in the study.[42] The patients were asked to wear Medtronic Zephyr BioPatch (an additional wearable device), for recording the physiological data for a period of up to 3 days.[42]
In diagnosing Central Precocious Puberty (CPP): Extreme Gradient Boosting (XGBoost) classifier used as the basic classifier to develop CPP diagnostic models. [43]

AI in Childhood Obesity: Obesity being a multifactorial, syndrome, is affecting paediatric population, but the development of Childhood obesity can be predicted as early as the age of 2 years with the use of ML. AI has advanced in developing food prediction models to keep maintenance of calorie deficit, along with development of various exercise games or mobile/ web based dance activities to enhance physical activity. One of such game developed was My Plate Pick, which has shown statistically significant results, in comparison to the control group. [44] Chatbots have been getting used in terms of providing personal recommendations and for the purpose of motivation to stay on calorie deficit, to enhance physical activity, to provide emotional support, and are available 24hours/ 7 days a week.[45,46]

In a study by Wang Bet et al, 14910 fundus images that were collected form 113 newborns (5-20 image/child), were analysed by trained DCNN for automated classification and retinal haemorrhage grading. The model was successful in classifying and grading with accuracy of 97.85%, 99.96%, 97.88% in grade 1,2 and grade 3 retinal haemorrhage respectively.[36]

Role of AI in Autism: Artificial intelligence could be used easily for supporting the communication and for the purpose of building social interaction in children with autism. [37,38] Various technologies such as robots, interactive games and virtual reality could be utilised in children with autism. AI robots are providing various engaging formats for children suffering from Attention deficit hyperactivety disorder (ADHD), such as Kaspar Robot has potential to improve social skills amongst children and RoboTherapy (Socially Assistive Robot) has been designed to improve social skills in ASD.[39]

In a multi-centre study, amongst 18-72 months of children, using three complementary modules cogna software, has outperformed in diagnosing Autism with sensitivity of 90%. [40]

The late diagnosis of Autism can impart long term implications amongst children and their families. AI could address many issues such as late diagnosis of Autism amongst many races, late diagnosis of autism amongst girls (approximately 1.5 years later in comparison to boys). FDA authorised Canvas Dx is helpful in initiating treatment early amongst autistic children. [41] This diagnostic device can be used in primary care settings that potentially decreases delay to treatment initiation and thus significantly improves the child's trajectory.

AI in Endocrine Diseases: Artificial intelligence is growing in the field of diagnosing endocrine diseases such as diabetes and precocious puberty, obesity amongst paediatric population as depicted in table 4,5.

Concerns with use of AI [47-49]: Clinical adoption of AI will be delayed if patients and practitioners will lack training to understand AI.

Therefore, standardisation of AI content need to be integrated in medical training.

1. Second concern could be ethical ambiguities as if malfunctioning occurs in AI, the impact could be difficult to tackle, and unintended results may occur such as major diagnosis could be missed. Therefore, ethical frameworks are under development to address such concerns of AI.
2. The need to develop policies for data storage and infrastructure, new codes of billing are to be approved by the national organisations.
3. These datasets can attribute in making decisions but the computation behind the models is complex.

For the purpose of developing and deploying AI in NICU, follows a workflow that includes [50]

Stage 1 Involves designing on the basis of developing neonatal networks, patients' needs and using neonatal specific datasets. Designing and establishing a protocol in which regular updates can be made and performance of the model can be tracked, and an expiry date setting has to be made.

Stage 2 Includes evaluation in which the validity of model can be assessed and soliciting feedback.

Stage 3 Includes validation that is proceeding cautiously before integrating in NICU, and using mulicentre and external cohorts for the purpose of generalizability.

Stage 4 Implementation (includes training programmes that should be comprehensive for all users). It also includes to take into consideration the work of recaliberation and implementing updates version.s

Stage 5 Monitoring for the purpose of detecting any bias and continuous vigilance at NICU.

Thus ensuring Ethical AI in neonatology includes proper governance and oversight by means of continuous review of risks, adherence to principles, auditing, advisory board involvement and regular tracking and documentation.

Cost of AI in paediatrics: More studies need to be conducted in terms of cost effectiveness of AI in paediatric population. AI is considered to be the cost effective method in terms of diagnosing a disease early and if a disease is diagnosed early, its complication can be prevented. Although the privacy and security is the main concern. In a study by Morrison SL et al, amongst 52000 neonates, in terms of incremental cost effectiveness, autonomous AI outperformed and had been the cost effective than telemedicine and ophthalmoscopy. The mean cost (95% CI and in dollars) have been 15030 for autonomous AI, 15063 for telemedicine, 15147 for Assistive AI, and 15392 for ophthalmoscopy.[51]

Limitation of the study: The study could have included more patient data and more machine learning tools used and are getting used in the field of paediatrics. In future the role of AI in the field of medicine could have been planned and done, with inclusion of more studies.

Conclusion

Health care delivery models are changing rapidly, and AI is greatly impacting the future of pediatric care. However, widespread integration of AI into pediatric care will require thoughtful solutions to privacy issues and complex data quality. Improvements in AI designs and its validation are needed for successful integration. To conclude, for the purpose of improving treatment and surveillance, physicians can work with assistance of AI techniques. AI presents opportunities to create a SMART NICU. Although multicentre collaboration is needed for developing AI methods in the field of neonatology. AI has to be implemented as a tool to enhance work force, not as a human judgement and expertise substitute.

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