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Application of Artificial Intelligence in pediatric Endocrinology: Current Scenario and Future Perspective

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Abstract

Background: *The management of commonly seen pediatric endocrine disorders such as short stature, early or delayed puberty and cretinism and juvenile diabetes etc. has shown significant growth in past decades. However, further improvements can be achieved by using novel digital techniques of artificial intelligence* ***(****AI****)****. Hence, this article has been aimed to provide a detailed overview of applications of AI in the field of pediatric endocrinology through available literature.*

Methodology: *A total number of 12 articles, published in peer reviewed journals, have been included to write the current review. The literature search was done by using electronic databases such as PubMed, Google scholar, Scopus. To increase precision in the search process, Boolean terms* ***(****AND/OR****)*** *were used to separate the keywords as well as medical subject headings* ***(****MeSH****)****.*

Results*: Though data scarcity has been found in this field of medicine regarding the AI application, certain studies have shown very promising results. After reviewing the literature, the utility of AI techniques in Pediatric Endocrinology have been discussed under the following headings: 1****)*** *Assessment and prediction of Growth, 2****)*** *Automation of Diabetes management, 3****)*** *Artificial Intelligence in Growth Disorders in Children 4****)*** *Application of Artificial Intelligence in T2DM 5****)*** *AI-led Diabetes Monitoring and Management in Children 6****)*** *Application of AI in childhood Obesity 7****)*** *and iv****)*** *Challenges and limitations*

Conclusion: *The AI techniques enable the physician with higher accuracy of diagnosis especially in the field of growth disorders and optimization of disease management through automation. Lack of awareness and funding, ethical issues, and the need to design new training programs in the curriculum are few challenges that need to be addressed for more clinical utility of AI in pediatric endocrinology.*

Key words: *Pediatric endocrinology, Medicine, Artificial intelligence, Machine learning, SANRA, Pediatric, AI and ML, Precision medicine.*

Introduction

Artificial intelligence is a term we come across quite a lot in recent years. It strives to simulate and expand human intelligence. **(**1**)** To many it gives the feeling that human jobs will be replaced by robots. The concept was first stated in the 1950s by Alan Turing who is considered the father of artificial intelligence. In a world where technology is rapidly advancing, artificial intelligence is also gaining great momentum. Furthermore, McCarther, one of the founders of the discipline of AI introduced it as "the science and engineering of making intelligent machines, especially intelligent computer programs" **(**2**)**. Therefore, it is defined as the ability of computers and machines to mimic human intelligence **(**3**)**. The main purpose of adopting AI in the healthcare field is to assist professionals in delivering improved quality in care services based on previous experiences, for instance identifying some disease symptoms through large database searches **(**4**)**. For example, smartphone sensors can measure the volume, assessing the tone, facial expressions, and pitch, calculate keyboard reaction time, and examine vital signs and many more. When these metrics are combined, it is possible to predict mental health behavior, pain, stroke, and heart attack **(**3**)**. It is said that once it is fully developed it will change dramatically the way medicine is practiced. **(**5**)** Great advances in computing power, increased digitization of data and extensive data collection has made the possibility of using AI in healthcare frequently **(**6**)** The science of pediatric endocrinology is a unique one in many aspects. Prevention is often the best course for many diseases that may occur. **(**7**)** Artificial intelligence is useful as it can mine data from electronic health records and augment the role of physician in disease diagnosis, management and clinical decision making. **(**8**)**

The role of a pediatric endocrinologist is to treat as well as prevent various diseases, Growth problems, such as short stature, Early or delayed puberty, Enlarged thyroid gland **(**goiter**)**, Underactive or overactive thyroid gland, Pituitary gland hypo/hyper function, Adrenal gland hypo/hyper function, Ambiguous genitals/intersex, Ovarian and testicular dysfunction, Diabetes, etc.…

This article aims to give an overview regarding the many applications of artificial intelligence in the field of pediatric endocrinology. The reporting of this study conforms to the Scale for Assessment of Narrative Review Articles **(**SANRA**)** guidelines, a brief critical appraisal for the assessment of nonsystematic articles. **(**9**)**

Methodology

A literature search was performed on October 10, 2022, that involved the identification of the search terms with respect to the application of artificial intelligence in nursing sciences in order to conduct this rapid review. Papers that described the application of AI in improving the functionality of medical diagnostic or therapeutic technologies among nurses or nursing care were included.

The databases searched for included PubMed, Google scholar, Scopus. Keywords used for the search included 'Pediatric endocrinology', 'Medicine', 'Artificial intelligence', 'SANRA', 'Pediatrics', 'AI', 'Precision medicine'. To increase precision in the search process, Boolean terms **(**AND/OR**)** were used to separate the keywords as well as medical subject headings **(**MeSH**)**.

Databases were searched for full-text, English language systematic and narrative reviews published between January 1st, 2010, to October 10, 2022. Articles published in languages other than English were not further considered. Articles published as a letter to the editor or conference abstract were also excluded.

Artificial Intelligence in Pediatric Endocrinology

Artificial intelligence has come a long way in healthcare due to its unique approach in diagnosis, evaluation, management, and treatment of a particular disease. Pediatric endocrinology is slowly adapting the use of new technologies and devices backed by Artificial Intelligence **(**10**)**. The pituitary gland plays a vital role in a child's growth and overall metabolism. Hormones are chemical signals which when not produced properly can cause growth disruptions and hormone imbalance **(**11**)**. Endocrine disorders such as growth disorders, diabetes mellitus, bone and mineral disorders, thyroid disorders **(**including thyroid cancer**)**, childhood obesity are a few areas of interest in current healthcare research.

The development of improvised screening tools for endocrine disorders may have clinical impacts, both in terms of effective prognosis of individual patients through disease detection at an early stage and the cost-effective allotment of public health resources by focusing on individuals with a high risk of disease and avoiding unnecessary testing in low-risk groups **(**12**)**.

Assessment and prediction of Growth

Assessment of growth failure

Pediatric disorders of impaired continuous growth are imposing significant hurdles to the patients themselves, their caregivers and healthcare professionals **(**13, 14**)**. Yet, there is still a lack of evidence regarding the management of those with short stature mainly in: a**)** early identification diagnosis of abnormal height and growth, b**)** early management by the administration of appropriate treatment, c**)** monitoring the efficacy of the chosen treatment, d**)** monitor the adherence of the patient to the therapy and patient support **(**11**)**.

Therefore, development of new technologies offered an improvement in diagnosing and treating pediatric patients with growth failure. For example, the FACE 2 GENE system that was developed to aid clinicians in diagnosing cases with genetic disorders affecting growth. This is a mobile application aiming to assist in targeting pediatrics with genetic disorders. It is based on comparing common facial features of the children to those with genetic disorders and variants. Firstly, the patient's photograph is converted to de-identified mathematical facial description and then compared **(**11**)**. A set of disorders with comparable morphology to the case is reported, and then artificial intelligence suggests which likely resembles the case **(**13**)**.

Mobile digital technology was introduced in this domain to track and record patient's adherence to the drug **(**drug delivery devices**)**. As a result, it will allow healthcare professionals to evaluate patient's patterns of administration over a period of time and identify potential adherence-related obstacles to overcome it. Therefore, it necessitates future advancements in AI and machine learning as they might predict patients' characteristics susceptible to poor treatment adherence and in need of special and modified treatment strategy to prevent or reduce poor adherence **(**11**)**.

Estimation of bone age

Another example relevant to the evaluation of growth disorders in pediatrics is the BoneXpert. It is an AI-based system used to estimate children's bone age based on an X-Ray of a hand, which can also be useful in predicting adult height.

A continuous enhancement of this system is being applied using machine learning **(**a subtype of AI**)**. An improved version **(**2**)** of BoneXpert is nowadays employed in different European hospitals. Furthermore, a recent publication assessed the version 3 that was released in 2019 compared to manual ratings. Findings showed that this automated system was more accurate in identifying bone age **(**15**)**.

Automation of Diabetes management

More recently, pre-diabetes and diabetes mellitus (pre-DM/ DM) are becoming more prevalent at a young age. Yet, evaluation of diabetes risk by a simple questionnaire screening tool is not yet developed for the youth (16). Vangeepuram et al. developed a youth diabetes risk screening tool and to evaluate if machine learning can help improve pre-DM/ DM screening performance on a large-scale dataset from the National Health and Nutrition Examination Survey (NHANES) (16). Findings showed that Data-driven ML-based methods yielded improvements over the screening guideline in identifying youth with pre-DM/ DM. Similarly, Hu et al. (17) designed a machine learning-based predictive model to identify adolescent diabetes in the National Health and Nutritional Examination Survey datasets with an AUC score of 71%.

Artificial Intelligence in growth disorders in children

The hormones produced by the pituitary glands are important for the growth and development in children (11). A pediatric endocrinologist is specially trained for treating children with hormonal disorders. Growth failure may be due to genetic mutations, acquired disease and/or environmental factors (18). Digital health technologies show promising results for improving outcomes in pediatric growth disorders by supporting personalization of care, from diagnosis to treatment and follow up (19) Short stature can be associated with a wide range of diagnoses including Turner syndrome, growth hormone (GH) deficiency, coeliac disease, inborn metabolic errors, chronic kidney disease and bone dysplasia (20). The development of a recombinant human growth hormone (r-hGH) proves to be an effective, readily available treatment modality for growth disorders.

A. Short stature

The r-hGH is currently approved in many countries for the treatment of short stature associated with GH deficiency (GHD), Turner syndrome (TS), Prader–Willi syndrome (PWS), chronic renal insufficiency (CRI), short stature home box-containing gene deficiency (SHOX-D) and being born small for gestational age (21). There has been an advancement in the r-hGH through an electromechanical auto-injector device "Easy pod" and a connected ecosystem "Easy pod Connect" consisting of a transmitter, software, and a secure, cloud-based data storage system. The use of this ecosystem enables adherence to be evaluated neutrally without any bias using real-world data obtained from this connected device (22).

B. Acromegaly

Acromegaly is a growth disorder often caused by prolonged secretion of excess growth hormone from a pituitary adenoma (23). Earlier two-dimensional (2D) photography was commonly used in acromegalic facial analysis. In recent years three- dimensional (3D) stereo photography has become immensely popular for facial analysis of post treatment acromegalic patients and can also be used for acromegalic extremities (24). Learned-Miller and team suggested a 3D morphable model to categorize the frontal face into different sub-groups in a semi-automated manner. 49 acromegaly patients and control were identified at an accuracy rate of 85.7% (25). Gencturk and team implemented a coupled system of local binary patterns (LBP) and Manhattan classifiers; this resulted in an accuracy rate of 97% (26). Larger datasets and machine learning methods increase the efficiency of facial recognition systems (27).

Application of Artificial Intelligence in Type 2 Diabetes Mellitus (T2DM)

Type 2 diabetes was predominantly observed among adults but the increase in incidence of obesity in children led to more cases of T2DM in younger individuals (28). Predictive analytics, machine learning and data mining approaches in T2DM are of major concern when it comes to diagnosis, management and other related clinical aspects.ML methods have gained immense popularity in healthcare research for automating the risk prediction process of T2DM, more precisely and with reduced medical cost. Artificial neural networks (ANNs), Logistic Regression (LR), Naive Bayes (NB), k-means clustering algorithm, Random Forests (RFs), Decision Trees (DT), and Support Vector Machines (SVMs)] are the most popular algorithms which can be utilized (29)

A. Support Vector Machine (SVM)

SVM is based on statistical learning theory which is also called Sequential Minimal Optimization (SMO). It is a learning system which uses a hypothesis space for linear functions in high dimensional space. SVM implements non-linear class boundaries by translating non-linear vectors into high dimensional feature space using a linear model (30)

B. K-means Clustering Algorithm

It is a machine learning algorithm that groups nearby points into clusters. There is no learning model construction in this algorithm since a new point is located by its distance from the cluster center or its arithmetic mean **(**31**)**

C. Naive Bayes (NB)

It's a classification algorithm which can determine class probabilities of Diabetes as normal or abnormal such as the probability that a given sample belongs to a particular class **(**32**)**

D. Random Forest (RF)

RF is a powerful machine learning method for categorization and regression which compares well with other state-of-the-art classifiers such as SVM **(**30**)**. The strengths of the RF approach are : 1**)** it does not overfit; 2**)** it is robust to noise; 3**)** it has an internal mechanism to estimate error rates, called out-of-the-bag **(**OOB**)** error; 4**)** it provides indices of variable importance 5**)**it can be used for data attribution and cluster analysis. These factors have led to an increased popularity of RF in the last few decades **(**33**)**.

E. Decision Trees (DT)

It is a tree structure-based model that describes the classification process based on input features. When the response variable is continuous it is used as a regression tree; and when the response variable is categorical it is used as a classification tree **(**30**)**. The steps in DT are - **(**i**)**construct a tree with its nodes as input features **(**ii**)** select the feature to predict the output from the input features **(**iii**)**repeat the steps **(**i**)** & **(**ii**)** to form sub trees based on features which are not used in the above nodes **(**34**)**.

F. Logistic Regression (LR)

It is a classification model which is extensively used in clinical analysis. It uses feasible approximations that help to understand the relationship between the dependent variable and one or more independent variables **(**35**)**. Logistic Regression is a huge AI calculation since it has the capacity to give probabilities and arrange new information utilizing ceaseless and discrete datasets **(**36**)**.

AI-led Diabetes Monitoring and Management in Children

The current era is a witness to a technological revolution for the management of diabetes in children through Continuous glucose monitoring (CGM) devices and different insulin delivery systems (such as insulin pumps, closed loop devices and automated insulin delivery devices) (37).

A. **Continuous Glucose Monitoring (**CGM**)** device - consists of a sensor **(**inserted under the skin**)**, a transmitter **(**receives glucose signal**)** and a receiver **(**receives glucose signal wirelessly and then displays the glucose value**)**

   The signal can be sent to a mobile phone via Bluetooth transmission **(**38**)**. These devices provide glucose data in two ways: in real-time **(**Medtronic or Dexcom**)** or by intermittent scanning **(**Abbott Freestyle Libre**) (**37**)**.

B. **Insulin Delivery Systems**- Insulin pumps or subcutaneous continuous insulin infusion **(**SCII**)** have been a dominant part of diabetes management modalities for many years. This pump therapy benefits by improving glycemic control, reduced hypoglycemia, and improved quality of life **(**37**)**

C. **Closed Loop Insulin delivery system (**Artificial pancreas technology**)** This system consists of a pump, an app and a control algorithm to imitate the pancreas by continuously monitoring glucose data and automating insulin delivery through a pump to match. This is popularly known as the "Artificial Pancreas Technology"**(**38**)**

Application of Artificial Intelligence in Childhood Obesity

Childhood Obesity is a widespread medical condition and presents as an intimidating obstacle for public health. Currently various technological interventions are available for childhood obesity prevention and treatment **(**39**)**.

1. The National Health and Nutrition Examination Survey **(**NHANES**)** is useful for monitoring national trends in obesity **(**40**)**.
2. The logistic regression model is used to assess the probability of body mass index in children **(**35**)**.
3. Technology based interventions such as internet and social media-based weight management programs, smartphone apps and active video games have been developed to educate overweight and obese children **(**41**)**
4. Exergaming- is using video games as a form of exercise which allows the children to become more active and disburse more energy **(**40**)**

5. Mobile Health (mHealth) apps are effective in achieving weight loss and subsequent maintenance. They successfully deliver behavioral therapy and promote physical activity and self-monitoring of diet, activities, and body weight (42).
6. Telemedicine is a virtual approach for obesity management through video consultations, education, and therapy sessions. Children prefer telemedicine so that they do not have to come face to face with the medical care professional since they are prone to shy away from the condition (40)

Future Perspective of Artificial Intelligence in Pediatric Endocrinology

Utilization of Artificial intelligence and Machine Learning will enhance diagnosis of endocrine disorders in future with higher accuracy, potentially avoid unnecessary investigations and reduce healthcare expenditures and facilitate better data digitalization Soon these benefits may revolutionize the clinical endocrine practice (10). Currently AI technologies like artificial pancreas for management of diabetes have already become a reality. Academically many efforts are required to accelerate further development of AI/ML technology in endocrinology (11). However, there is no focus on training programs for endocrine subspecialties, and there is no arrangement of necessary education for trainees to feel confident in the use of these technologies for diagnosis or research. There is a need to spread awareness, facilitate crowd funding , introduce these concepts into training programs and encourage further research in this exciting new branch of endocrinology and metabolism (20).

Conclusion

Digital health and computer-based technologies are rapidly altering healthcare services to make medicine much more patient-centered and personalized. At a more advanced level, various digital health tools are being introduced that can provide better identification of disorders and promote effective engagement between clinicians and patients (10) Growth monitoring applications for phones and tablet computers are being developed, based on longitudinal growth studies. Thus, rapid advances in computing and artificial intelligence technologies are providing many new tools for pediatric endocrinologists (11) New eHealth tools can help pediatric endocrinologists by making their clinical assessment and patient management more efficient and precise. Most tools are currently designed to be used by clinicians, although future directions may need to explore new ways in which patients can have a direct access to the technologies.

However, these digital technologies should provide better communications between clinicians and patients. Treatment decisions based on these new techniques should always be patient-centered (25)

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