Clinically Applicable Artificial Intelligence for Retinal Imaging based Teleophthalmology for Primary Eye Care in India: A Review

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1 Introduction

Universal health care is the third sustainable development goal of the United Nations[UN]. The World Health Organization (WHO) Global Action Plan (GAP) 2014-19 focuses on achieving Universal Eye Health Coverage (UEHC) using Primary Eye Care (PEC) approach[WHO]. In India, Comprehensive Eye Care (CEC) can be given only using the health system approach[35]. But, there is a severe gap in the availability of ophthalmologists in India, leading to underserving and unserving a huge population of India, predominantly in the rural side[39]. Some of the barriers in the rural and suburban areas to accessing quality eye care are the loss of time, lack of transportation, issues in the delegation of household responsibilities, and loss of income[21].

Global estimates show that by 2020, the prevalence of age-related macular degeneration will be 32.1 million, while that of glaucoma and diabetic retinopathy will be 15.4 million and 12.9 million, respectively. All these causes can be detected and treated early using retinal imaging[25]. Ophthalmology is a discipline that relies on visual information for clinical decision-making, which makes it ideal for telemedicine[17]. Telemedicine is known to reduce the burden of eye disease[32;38]. Telemedicine has evolved from simple telephonic consultations to asynchronous online video conferencing with clinicians[47;80]. This progress is further strengthened by cloud computing, increased storage capacities, advanced computing power, and enhanced storage, retrieval, and analysis of clinical data[2]. In addition, artificial intelligence (AI) as an assistive technology, especially in medical imaging, is revolutionizing the field of healthcare[18;55;23;3]. This is especially true of ophthalmology, where retinal imaging, telemedicine, and AI address various causes of preventable blindness[69;30;43;33]. Retinal images can be captured digitally and transmitted along long distances using the store-and-forward system[105].

In spite of progress in retinal imaging, telemedicine, and artificial intelligence, no comprehensive model has been developed, tested, validated, and deployed in resource-poor settings like semi-urban and rural India. This review focuses on developing a primary eye care model using a health systems approach that utilizes retinal imaging, artificial intelligence, and telemedicine[10].

2 Methods

Between January 2020 and March 2020, a scoping review of the literature was done in open databases (Google Scholar, Scopus, PubMed, Web of Science, and Medline) using the following search terms: "Teleophthalmology", "Retinal Imaging and AI," "Teleophthalmology and AI," "AI in ophthalmology" and "Telemedicine in ophthalmology." Papers published in English within the last 5 years were chosen based on relevance. Duplicates were removed. Analysis was done using a 'best-fit' framework-based synthesis approach[22]. Articles were analyzed, and relevant key insights were derived from them and categorized under the themes chosen apriori (namely, retinal imaging using a fundus camera, automation of retinal image analysis, and teleophthalmology models in India). The insights were further subjected to secondary analysis to find connections[82]. A final framework was developed based on the similarities, differences, and relationships between categories[27].

3 Results

Table 1 shows the overall framework of the findings before and after synthesis. A model was developed based on the findings. The findings and the model are elaborated under discussion.

Table 1: Overall framework of the findings before and after synthesis

Apriori themes	
1. Retinal imaging using fundus camera 2. Automation of retinal image analysis 3. Teleophthalmology models in India	
Themes derived after synthesis	
Themes	Concepts
Clinical potential of Retina	1. Anatomy of retina 2. Retinal findings in various cardiovascular, cerebrovascular, neurodegenerative and non-communicable eye diseases
Retinal Imaging	1. Optics of retinal imaging using fundus camera 2. Evolution of fundus camera
Teleophthalmology in India	1. Successful models in India 2. Use of local employed youth as technicians 3. Benefits of teleophthalmology in India
Use of technology in teleophthalmology	1. Cloud 2. Artificial intelligence in Retina 3. Clinical Decision Support Systems
Challenges associated with merging teleophthalmology, AI and Cloud in India	1. Lack of awareness and acceptance among patients and doctors 2. Existing structural and institutional barriers

4 Discussion

The discussion of findings is done in two parts; a) findings from the analysis and b) proposed teleophthalmology model based on AI-assisted retinal imaging.

a) Findings from the analysis

Clinical Potential of Retina

Retinal vasculature is analogous to cerebral vasculature with a common embryological origin and shares similar anatomic and physiologic properties, while the retina is an extension of the diencephalon[85]. Any change in the cerebral vasculature, therefore, can be noticed in the retinal vessels too[59]. The unique property of retina is that it can be noninvasively and directly visualized in vivo[60]. This brain-eye connection and ease of visualizing the retina make it a potential tool for screening and diagnosis. A number of studies have been reported that demonstrate a correlation between retinal vasculature and systemic illness, cerebrovascular diseases, cardiovascular diseases, neurodegenerative diseases, and psychiatry.

Diabetes, hypertension, and obesity showed narrower central retinal arteriolar equivalents (CRAE) and wider central retinal venular equivalents (CRVE)[53;52;67;28;94]. Studies show that retinal microvascular changes reflect the severity and duration of hypertension[97]. Retinal microvascular findings in hypertension may be distinct from those of atherosclerosis[101]. The Atherosclerosis Risk in Communities Study (ARIC) showed that cognitive impairment is independently associated with retinopathy, exudates, and microaneurysms[102]. In stroke, studies show that retinal microvasculature reflects the condition of the cerebral vasculature[4;78;54;66]. Research indicates that retinal microvascular abnormalities may provide independent information regarding cardiovascular risk[100] and as an indicator for cerebrovascular risk[99]. Therefore, retinal imaging can be used for cerebrovascular-risk stratification[98] and can be used for screening in the clinical scenario and epidemiological research[96].

Changes in small cerebral arteries correlate with changes in retinal arteries[40]. In Alzheimer's disease, there is a reduction in the nerve fiber layer of the retina and subsequent dysfunction[58]. There is also ganglion cell loss in the central retina[14]. Also, neurons are lost in the retina with an increased astrocyte/neuron ratio[13]. Studies recommend the addition of neuronal degeneration in the ganglion cell layer (GCL) as a part of the neuropathological changes in Alzheimer's disease[12]. Also, research shows the importance of retinal imaging in screening patients of dementia and other neurodegenerative disorders[81]. In Parkinson's disease, a reduction in the retinal microvascular density suggests the link between retinal microvascular abnormality and neurodegeneration[41]. In multiple sclerosis, a disproportionate thinning of inner and outer nuclear layers of the nerve fiber layer of the retina is seen that is independent of the optic nerve pathology[63].

In psychiatry, retinal vascular features have been studied as potential biomarkers[5]. Research indicates that retinal examination can be used as a biomarker of neural pathology and progression of disease in Schizophrenia[72]. Abnormalities of the retinal layer that can be related to clinical findings and visual impairment have been reported too[65]. In bipolar disorder, there is a thinning of the macular retinal nerve fiber layer, ganglion cell layer, inner plexiform layer, and inner nuclear layer[26]. Therefore, retinal nerve fiber layer thickness can be used for assessing the severity and duration of bipolar disorder[46].

Retinal imaging using fundus camera

Fundus camera, used for retinal imaging, is a complex optical system designed to address the specific challenge of sharing the common optical path for both illumination and imaging[71;51;36]. Also, the retina is a minimally reflective surface which makes the power of the back reflections from the shared optics of the illumination and imaging paths greater than the power reflected by the retina[31;20;8]. Retinal imaging using a fundus camera has evolved from the traditional monocular indirect ophthalmoscopy to the latest systems of applying filters to camera for autofluorescence, fundus fluorescein angiography, and indocyanine green angiography and automated analysis[37;70;84;106]. This has resulted in better image quality, ease of use, portability, field of view, and cost. Today there are a number of companies that manufacture a range of devices in this segment, including hand-held devices and smartphone-based imaging devices[56]. Modern devices are especially suited for mass screening, remote diagnosis, and telemedicine[56;15].

Teleophthalmology in India

Teleophthalmology in India has successful projects being implemented for primary care as well as research with the support of the Department of Information Technology (that formulated the Standards for Telemedicine Systems), Ministry of Health and Family Welfare (that constituted the National Telemedicine Task Force) and ISRO[48;11]. The teleophthalmology projects provide basic eye care as well as specialty care (ROP, ARMD, DR, and Glaucoma, among others). Outcomes assessment shows that teleophthalmology models provide similar outcomes to traditional methods of healthcare along with larger coverage, improved accessibility, reduced time and cost, as well as high satisfaction level and acceptance[76].

The Chunampet Rural Diabetes Prevention Project (CRDPP) aimed at comprehensive diabetes screening, prevention, and treatment, combines telemedicine with personalized care for 42 villages in rural India. A mobile van with satellite connectivity is deployed equipped with retinal imaging. Local unemployed youth are recruited and trained to be eye technicians for capturing images. Images are then transmitted via satellite to a base hospital in Chennai. The ophthalmologist then interacts with the patients using video conferencing[49;61].

Another exclusive teleophthalmology project by Sankara Nethralaya Medical Research Foundation, Chennai, uses a mobile van equipped with an in-built ophthalmic examination facility connected with the base hospital via satellite. This is taken care of by a social worker and an optometrist. Preliminary screening for eye disease patients is done through medical camps. Patients requiring care, along with the optometrist, interact with the ophthalmologist using synchronous video-conferencing[61;87]. A similar model by Aravind Teleophthalmology Network has a mobile van for screening diabetic patients that connects to the experts via satellite[61;9]. These teleophthalmology models have also been instrumental in continuing medical education[61].

A public-private partnership (PPP) model is used in the Karnataka Internet Assisted Diagnosis of Retinopathy of Prematurity program (KIDROP) project, where non-physician graders were deployed to remote neonatal intensive care units (NICUs). The technical abilities of the graders were done using an indigenously developed 20-point score (STAT score). Based on the score, they were between Levels I to III. These technicians took images using a portable wide-field retinal digital camera, graded them using a three-way algorithm, and uploaded them to a server interpreted by ROP specialists using a customized app on their smartphones. Management decisions were made based on the three-way algorithm validated by the experts on whether to discharge, follow up or refer the neonate to a specialist[91;90;92;89;88].

Use of technology in teleophthalmology

Cloud, Artificial Intelligence (AI), and clinical decision support systems are the relevant technology in ophthalmology that can be effectively deployed in telemedicine models. A retrospective cohort study in the UK studied the implementation of a cloud-based referral platform to improve communication between optometrists and ophthalmologists to reduce unnecessary referrals. The study showed that the implementation of the cloud reduced the need for referrals by half while providing digital-first rapid-access eye care to the patients and enhanced communication between various service providers[34]. Another study reported a cloud-based electronic medical record for scheduling, tracking, and documenting examinations and treatment of Retinopathy of Prematurity in NICU with an improved proportion of eligible neonates getting their scheduled eye examinations in a timely manner[6].

A review showed that very few clinical decision support systems (CDSS) are in use. Out of the existing systems, most of the CDSS is for the posterior pole of the eye, predominantly for Diabetic Retinopathy (DR) using retinal imaging. The study suggested that an app of CDSS in ophthalmology will be useful for doctors and teachers, especially when combined with EHRs, cloud storage, and data mining[19].

The availability of thousands of digital retinal images has enabled the utilization of AI in ophthalmology, especially deep learning (DL). Deep learning algorithms applied to retinal images have detected, localized, and quantified diabetic retinopathy, retinopathy of prematurity, glaucoma, and age-related macular degeneration[83]. The AI-based analysis of retinal images, many with varying sensitivity, specificity, validity, reliability, interpretability, and applicability. Fully automated systems have been approved for use in DR screening. Such systems can be used for screening, diagnosis, and follow-up in major eye diseases for individuals as well as for the community. These can also be deployed for personalized health care for patients apart from empowering the ophthalmologist with an enhanced diagnostic and therapeutic accuracy[68].

Challenges associated with merging teleophthalmology, AI and Cloud

There is an overall lack of awareness and acceptance of new technology by patients and doctors[16]. Apart from this, several structural and institutional barriers affect the development, deployment, validation, and acceptance of technology[74]. There are also issues related to data privacy, cyber security, and related regulations that are yet to be defined clearly in India[7].

b) Proposed teleophthalmology model based on AI-assisted retinal imaging

Telemedicine systems have been shown to greatly benefit the health-service provider as well as the patient by cutting down the treatment costs, delivering satisfaction, and providing personalized care[77;64;75;62;73;44;24;104;1]. Based on the review, we propose an asynchronous telemedicine model based on AI-assisted retinal imaging. In the Asynchronous Store-and-Forward Telemedicine (ASFT) model, patient health data is digitally collected from remote locations by trained personnel or automated procedures and sent to an online facility; generally, a Picture Archiving and Communication System (PACS) or Telemedicine server for analysis and interpretation by the health-service provider. The diagnosis is made available to the referring physician for informing and treating the patient.

Due to soft constraints on network availability, ASFT models can be successfully employed in settings with intermittent net connectivity or bandwidth bottlenecks, such as in wilderness or environments requiring high mobility. It is also desirable when specialized, but scarce medical staff expertise is responsible for patients scattered over a large area or in pandemics like Covid-19. It helps optimize medicine delivery, reduce patient waiting time, prioritize scarce resources, and deliver care to a larger population without additional investment. The principal usage of ASFT services is for diagnosing and evaluating patient examination reports.

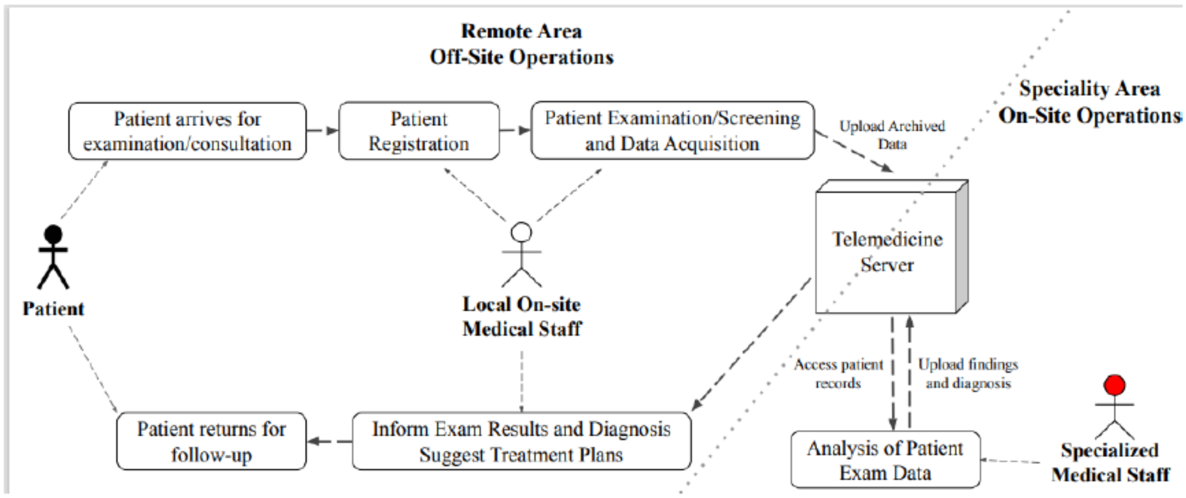

Figure 1: Operational workflow in an asynchronous store-and-forward telemedicine model

Image 1 shows a medical diagnosis workflow using ASFT model[29]:

1. A patient is examined at a remote medical facility by trained personnel.

2. The examination data is digitally collected and stored on telemed-server and later allocated to participating medical staff for analysis.

3. The doctors analyze the health reports and upload their findings to the server.

4. This health data is then made available to the assigned practitioner to deliver diagnosis information and appropriate treatment to the patient.

The proposed ASFT model will be deployed in the context of a teleophthalmology screening system. It would be a semi-automated model that leverages Artificial Intelligence (AI), especially Deep Learning (DL) and Machine Learning (ML), powered intelligent modules to aid practitioners in diagnosis. These modules would be crucial in its use-case as a point-of-care screening facility and speed up the delivery of care.

Real-time disease detection from retinal images with modern-day AI is still a challenge. Thus, a powerful AI with great accuracy and explainability is necessary to make this model successful.

The following salient features are expected to be a part of this model;

- DL-based primary-level screening of vision-threatening diseases. The abnormal cases encountered can be immediately referred to advanced clinical care facilities
- Non-mydriatic imaging for patient convenience and reduced scan times.
- DL modules will provide multidimensional annotations for highlighting ocular abnormalities; deliver the diagnosis meaningfully like a comprehensive ophthalmologist.
- Secondary Clinical Parameters: Relevant clinical data, such as past treatments, are utilized in intelligent diagnostic algorithms.

There are various issues to account for when deploying AI applications in the real world[42;57]. From data collection to model inference, high quality of data must be maintained for a fair performance[79;93] as training data directly impacts the performance. Other challenges and limitations include network connectivity, adoption by the patients and providers and insurance companies, and reimbursements[45;103;50].

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