Power System Technology
ISSN:1000-3673

Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

The Development of Optics in Modern Technology (Nano-Artificial Intelligence) In the Treatment and Early Detection of Diabetic Retinopathy in Saudi Arabia

Samir Sulaiman Bassir[1], Azza Abdulkhalig Alzahrani[2], Abdulmjaeed Abdulrahman Alzahrany[3], MANSOUR Abdullah Hakami[4], Amal Theyab Alghamdi[5],

Ophthalmologist -King Faisal Hospital – Makkah[1]

Optometrist - Jeddah Eye Hospital [2]

Optical laborlory technician, Al-Makhwah General Hospital Albaha, Ministry of Health, Kingdom of Saudi Arabia[3]

Technician-optics, Al-Makhwah General Hospital Albaha, Ministry of Health, Kingdom of Saudi Arabia[4]

Optometrist, Al-Makhwah General Hospital Albaha, Ministry of Health, Kingdom of Saudi Arabia[5]

ABSTRACT

Diabetic retinopathy (DR) remains a leading cause of preventable blindness, yet limitations in current screening methods and treatment strategies hinder timely diagnosis and effective management. Existing studies in Saudi Arabia have largely focused on conventional diagnostic and therapeutic approaches, with insufficient integration of advanced optical artificial intelligence (AI) systems and nanotechnology-based interventions. This study aimed to evaluate the role of optics-driven AI in the early detection of DR and to investigate the efficacy of nanocarrier-assisted therapy for retinal protection. A diagnostic cohort of 500 patients underwent retinal imaging analyzed by AI and human graders against ETDRS reference standards, followed by logistic regression to identify predictors of referable DR. In a randomized pilot trial, 60 patients were assigned to nanocarrier or standard therapy arms and monitored for changes in central subfield thickness (CST) and best-corrected visual acuity (BCVA) over six months. The AI system achieved higher sensitivity than human graders (96.6% vs. 81.8%, $p < 0.001$) with an AUC of 0.997. Elevated HbA1c (OR = 1.41, $p < 0.001$) and diabetes duration (OR = 1.05, $p = 0.003$) were significant predictors of referable DR. Nanocarrier therapy achieved greater CST reduction (–18.7 µm, $p = 0.028$) and BCVA improvement (+2.6 letters, $p = 0.041$) without additional safety risks. These findings demonstrate the value of integrating AI-based screening with innovative nanotechnology to enhance early detection and treatment of DR.

Keywords: artificial intelligence, diabetic retinopathy, nanocarrier therapy, optical imaging, Saudi Arabia

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

INTRODUCTION

Diabetic retinopathy (DR) is one of the most serious microvascular complications of diabetes mellitus and the major cause of preventable blindness in the working-age population of the world [1]. In 2021, the International Diabetes Federation (IDF) estimated that 537million adults have diabetes, with a projected rise to 643 million by 2030. Almost a third of them develop some form of DR in this cohort, and a significant percentage advance to stages where it can cause vision loss unless early detected and treated [2]. The incidence of DR is especially worrying in Saudi Arabia, where the incidence of diabetes is among the highest in the world; according to recent epidemiological research, the proportion of diabetic patients with retinal complications can reach up to 36 [3]. This situation highlights a pressing need to identify the problem as early as possible and implement therapeutic interventions that would address the Saudi healthcare setting.

In the last 20 years, the development of optical imaging and artificial intelligence (AI) applications has revolutionized ophthalmology by providing clinicians with new methods of detecting, grading, and monitoring DR [4]. Optical coherence tomography (OCT) and fundus photography have already become the standard of care in clinical and research practice, but an even more recent development is the introduction of nano-optics and AI-based algorithms combining high-resolution imaging with automatic interpretation [5]. Nanotechnology imaging can provide opportunities to improve the resolution, contrast, and functional understanding of the observations in comparison to the traditional modalities, and AI systems can process image data in large volumes with high sensitivity and specificity [6].

The range of this research goes beyond national and foreign borders. Countries with intensified diabetes rates are seeking less expensive, scalable interventions of DR screening and treatment globally [7]. Already, the United Kingdom, Singapore, and the United States have conducted AI-based DR screening programmes with promising results, though these are more often based on traditional imaging and do not feature nanotechnology [8]. There are also national diabetes prevention and screening programmes in Saudi Arabia, which are not evenly distributed, and those in rural areas are inaccessible to ophthalmic specialists. This gap underlines the pressing necessity of new, affordable technologies that can be used to supplement the current healthcare systems [9].

The literature gives solid reasons to support the use of AI in screening for DR. A number of deep-learning systems are diagnostic to the level of retinal experts, with sensitivities reaching over 90 percent and an area under the curve (AUC) of over 0.95. As a case in point, [10] created a deep-learning algorithm, which had a sensitivity and specificity of over 90% in identifying referable DR in large populations; [11] validated an AI system in multi-ethnic populations in Asia with high diagnostic accuracy. These articles highlight the AI maturity in use as a diagnostic tool. At the therapeutic end, nanomedicine has been used to

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

target anti-VEGF agents, corticosteroids, and other therapeutic molecules into the retina, thereby enhancing the bioavailability of the drug and reducing systemic toxicity [12]. Although these breakthroughs have been reported in several international contexts, little evidence is available in Saudi Arabia.

The importance of this study is that the fields of optics, nanotechnology, and artificial intelligence were combined into a single framework to detect and treat DR at its early stages. The combination of these fields of study makes the study respond to two important ophthalmology priorities, namely increasing the accuracy of the diagnostic process and the effectiveness of therapeutic outcomes [4,13]. Such innovations have particular promise in a country like Saudi Arabia, where prevalence rates of diabetes are growing at an alarming rate and healthcare systems are strained to increase the number of people receiving screening [14]. Thus, the research addresses both the local and general healthcare requirements and is likely to become an excellent example of the implementation of the latest optical and AI-enhanced technology in ophthalmology [15].

The research has been conducted in order to address a knowledge and practice gap. Although AI-based diagnostic solutions to DR are internationally validated, little evidence is presented concerning the use of AI systems in Middle Eastern populations and Saudi Arabia, in particular [16]. In addition, the multifaceted benefit of combining nano-optics and nanocarrier-based treatments with AI has not been studied systematically. Earlier research has focused either on diagnostic innovations alone or therapeutic ones, without considering diagnostic integration [17]. This piecemeal methodology leaves unanswered the question of how best to formulate a comprehensive framework of DR management that cuts across both the early detection and the treatment [18].

The following research questions were used to develop the methodological framework of the present study: (1) Can nano-AI-based optical systems closely or better outperform human graders in the detection of referable DR in Saudi patients? (2) What clinical, demographic, or biochemical predictors play the greatest role in the risk of referable DR in this population? (3) Does nanocarrier-based intravitreal therapy give better structural and functional outcomes than conventional therapy in patients with DR? The diagnostic accuracy assessment and the interventional pilot trial aspects of the study were based on these questions.

The study goals are thus trifold. First, to determine the diagnostic accuracy of AI combined with the latest optical technologies in the identification and grading of DR as compared to the traditional manual grading [19]. Second, to determine the independent predictors of referable DR, including the level of HbA1c, length of diabetes, and other systemic variables, through the use of strong statistical models. Third, to determine the effectiveness and safety of nanocarrier-based therapeutic intervention in enhancing structural

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

(central subfield thickness) and functional (best-corrected visual acuity) outcomes in patients with DR. The approach will be an integrated diagnostic cohort study interventional pilot trial that will allow the study to have a holistic assessment in terms of detection and treatment.

METHODOLOGY

The current research focused on the issue of late diagnosis and the narrowness of treatment options for diabetic retinopathy (DR) in Saudi Arabia. Combining nano-optical imaging with artificial intelligence (AI) diagnostic algorithms and piloting nanocarrier-based therapies, the study would find out whether the systems could be used to improve early diagnosis and increase therapeutic outcomes over current standards.

The study aimed at three goals: initially, determining the diagnostic accuracy of the combined approach of advanced optical imaging with AI algorithms to detect the early signs of the disease in patients with referable DR; second, determining the safety and initial efficacy of the nanocarrier-based intravitreal therapy in diabetic macular edema (DME); and third, determining the obstacles hindering the adoption of these technologies in the Saudi healthcare system. These aims directly responded to the main research question of whether nano-optics and AI would allow enhancing the possibility of early detection and treatment in local conditions.

The research was done in three tertiary ophthalmology centres located in Riyadh, Jeddah, and Eastern Province, selected because they have retinal imaging facilities, a high volume of patients, and the ability to provide advanced diagnostics and intravitreal therapy. Every site had electronic health records and had a well-developed clinical research infrastructure. There was a convergent mixed-method. The diagnostic accuracy study used a prospective cross-sectional design to compare the AI-based classification of DR with the Early Treatment Diabetic Retinopathy Study (ETDRS) reference standard. As a treatment, one randomised controlled pilot trial was conducted on a nanocarrier formulation of DME. To determine the feasibility and acceptability, a qualitative aspect (semistructured interviews with clinicians and patients) was incorporated. This design was explained by the fact that it was possible to evaluate the level of diagnostic performance and therapeutic effect quantitatively and also discuss the translation into Saudi practice.

Its population was the people, both adults (≥18 years) with type 1 or type 2 diabetes, who were visiting ophthalmology clinics. Sampling was done sequentially in order to reduce bias. In the diagnostic study, sensitivity was estimated with a sample size of 95 confidence, hence the calculated sample size. Based on the sensitivity of 90% and the prevalence of DR at about 30% a minimum of 449 participants was needed; to consider the chance of attrition, 500 participants were targeted. To conduct the pilot trial, 60 with centre-involved DME were randomised 1:1 to nanocarrier therapy or standard care. Gradable retinal images, participants

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

who agreed to participate, and medical soundness were the inclusion criteria; factors that excluded participants were conditions that caused issues with imaging or the safety of treatment.

Supplementary imaging equipment consisted of spectral-domain optical coherence tomography (OCT), high-resolution adaptive optics OCT when available, and fundus photography. Images were analyzed with AI pipes (TensorFlow-based), producing referable DR probability scores. Masked reference grading was done in a certified reading centre. To treat the patients, intravitreal injections of nanocarriers were made under sterile conditions and followed at baseline, 1 week, 1 month, 3 months, and 6 months. Clinical outcome measures were OCT-central subfield thickness and best-corrected visual acuity (BCVA). Intraocular pressure, inflammation, and adverse event reporting were all a part of safety monitoring. REDCap electronic case report forms were used to capture the data. Imaging and AI workflow piloting of 30 patients was done to clarify protocols.

The most important diagnostic variable was referable DR (moderate or more non-proliferative diabetic retinopathy or DME). The results of AI classifiers were probability scores, categorised at set thresholds. The major endpoint in the treatment arm was the mean change in central subfield thickness, with the secondary endpoint being BCVA. Adverse event frequency was taken as a measure of safety. Cohen's κappa was used to determine inter-grader reliability. The reliability of measurements was guaranteed by the use of device calibration logs.

Diagnostic accuracy parameters (sensitivity, specificity, positive predictive value, negative predictive value, and area under the receiver operating characteristic curve) and 95 percent confidence intervals were determined. The McNemar test was used to compare paired proportions (AI vs. reference), whereas the DeLong test was used to compare AUCs. Generalised estimating equations had considered within-patient clustering. Evaluation of calibration was done using the Brier score and calibration plots. Subgroup analysis was conducted on performance based on diabetes length and image modality. To analyse the pilot trial, descriptive safety data were summarised, and exploratory efficacy was analysed with mixed-effects linear models of repeated central subfield thickness and BCVA data. Sampling sizes. Planning of future confirmatory trials was informed by variance estimates. All the analyses were conducted in R (pROC, lme4) and SPSS.

Institutional review boards of all participating centres, as well as the Saudi National Committee of Bioethics, gave ethical approval. Informed consent was obtained in writing by all participants. Data was kept encrypted and de-identified using codes to ensure confidentiality. The adverse events of the treatment pilot were reviewed by a Data Safety Monitoring Board. GOOD Clinical use: The investigational nanocarrier was subjected to Good Laboratory Practices preclinical safety testing before clinical use. The paper admitted

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

bias. Recruitment may be less generalisable to population-wide screening since clinic-based recruitment was used; however, multi-centre sampling overcame this. Standardised acquisition protocols were used to deal with image quality variation. Site-specific differences limited AI generalisability, and this was handled by external validation. The pilot trial did not have an efficacy power, and could only reach a conclusion on safety and feasibility. The long-term safety of the nanomaterials was still a question of time and demanded a prolonged follow-up. This methodology was a combination of rigorous diagnostic accuracy testing, testing of therapeutic interventions at an early stage, and analysis of implementation to establish the role of nano-optics and AI in managing DR in Saudi Arabia. The design focused on accuracy, repeatability, and ethical rigour, and it was necessary to ensure the results were useful in informing clinical implementation and subsequent large-scale trials.

RESULTS

Baseline Characteristics

The diabetic arm of the study involved 500 diabetic patients. The age mean was 55.0 10.2 (range: 32 76) (275 males, 55.0% and 225 females, 45.0%). The mean time span of diabetes was 8.857.4 years, and the mean glycated hemoglobin (HbA1c) was 8.021.48%. The average central subfield thickness (CST) on optical coherence tomography images was 419 82 42 mm, and the average best corrected visual acuity (BCVA), 72.4 86 ETDRS letters.

Table 1: Baseline demographics and clinical characteristics (Diagnostic cohort, n = 500)

Variable	Total (n=500)	Referable DR (n=155)	Non-referable DR (n=345)	p-value
Age, years (mean ± SD)	55.0 ± 10.2	56.8 ± 9.8	54.2 ± 10.5	0.031*
Male, n (%)	275 (55.0%)	88 (56.8%)	187 (54.2%)	0.614
Diabetes duration, yrs (mean ± SD)	8.8 ± 7.4	11.6 ± 8.1	7.4 ± 6.8	<0.001*
HbA1c, % (mean ± SD)	8.02 ± 1.48	8.65 ± 1.51	7.71 ± 1.39	<0.001*
CST (µm, OCT)	419 ± 42	448 ± 50	404 ± 37	<0.001*
BCVA, ETDRS letters	72.4 ± 8.6	68.2 ± 9.4	74.5 ± 7.8	<0.001*

*Statistically significant ($p < 0.05$).

Referable diabetic retinopathy (DR) was most prevalent at the rate of 31.0 (n = 155), and non-referable DR was the highest with 69.0 (n = 345). Patients with referable DR were found to have a longer duration of diabetes (11.6 ± 8.1 vs. 7.4 ± 6.8 years, $t = 5.11$, $p < 0.001$) and a higher level of HbA1c (8.65 ± 1.51 vs. 7.71 ± 1.39, $t = 6.09$, $p < 0.001$) than those with

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

no referable DR. The CST was higher in the case of referable DR (448 ± 50 µm vs. 404 ± 37 µm, t = 9.83, p < 0.001), but there was a significant difference in the BCVA (68.2 ± 9.4 vs. 74.5 ± 7.8 letters, t = -8.41, p < 0.001). The sex difference was not significant (2 = 0.26, p = 0.614).

Performance of AI and Human Grader

The artificial intelligence (AI) system, compared to the ETDRS reading center, as the gold standard, correctly identified 143 true positives (TP), and 339 true negatives (TN), with 13 false positives (FP) and 5 false negatives (FN). This translated to a sensitivity level of 96.6% (95% CI: 93.1 98.7), a specificity level of 96.3% (95% CI: 94.0 97.9), positive predictive value (PPV) of 91.7% (95% CI: 86.6 95.3) and a negative predictive value (NPV) of 98.5% (95% CI: 96.7 99.5). The precision of the AI system was 96.4 in general.

Table 2: Diagnostic performance of AI vs human grader (vs ETDRS reference standard)

Metric	**AI system**	**Human grader**
Sensitivity	**96.6%**	81.8%
Specificity	96.3%	**97.4%**
Positive predictive value	91.7%	93.1%
Negative predictive value	**98.5%**	92.7%
Accuracy	**96.4%**	92.8%
AUC (95% CI)	**0.997 (0.994–0.999)**	0.979 (0.967–0.990)

AI significantly outperformed human grader in sensitivity (McNemar's $\chi^2 = 15.2$, $p < 0.001$).

Comparatively, the human grader scored 121 TP and 343 TN grades, 9 FP and 27 FN. This gave a sensitivity of 81.8% (95% CI: 74.787.6), specificity of 97.4 (95% CI: 95.4-98.7), PPV of 93.1% (95% CI: 87.5-96.8), and NPV of 92.7% (95% CI: 89.5-95.0). The total diagnostic error was 92.8%. The AI system had better sensitivity than the human grader (96.6% vs. 81.8, X 2 = 15.2, p = 0.001) and slightly less specificity (96.3% vs. 97.4, chr = 0.87, p = 0.351). ROC analysis showed that the AI system has an AUC of 0.997 (95% CI: 0.994-0.999) and the human grader has 0.979 (95% CI: 0.967-0.990). The bootstrap analysis (1,000 samples) proved the higher AUC performance of AI, and non-overlapping confidence intervals showed the statistical robustness.

Predictors of Referable DR

The logistic regression modeling was conducted to determine the predictors of referable DR. HbA1c, diabetes duration, and age were added to the model as covariates. The regression

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

model was statistically significant (26 = 42.7, p < 0.001) and it had a value of 23% explained variance (Nagelkerke R 2 =0.23).

Table 3: Logistic regression predicting referable DR (n = 500)

Predictor	OR (95% CI)	p-value
HbA1c (%)	1.41 (1.21–1.65)	<0.001*
Diabetes duration (per year)	1.05 (1.02–1.09)	0.003*
Age (per year)	1.01 (0.99–1.03)	0.180

Model χ^2 = 42.7, p < 0.001. HbA1c and diabetes duration were independent predictors of referable DR.

- **HbA1c:** One unit increase in HbA1c was linked with a 41 percent rise in the likelihood of referable DR (OR = 1.41, 95% CI: 1.21 -1.65, p < 0.001).
- **Duration of diabetes:** The odds of referable DR with each additional year of diabetes duration were 5% higher (OR = 1.05, 95% CI: 1.02109), P = 0.003).
- **Age:** Age was not a significant predictor of referable DR (OR = 1.01, 95% CI: 0.99103, p = 0.180).

Nanocarrier Pilot Trial

Sixty subjects were randomized by splitting them (n = 30) each to nanocarrier (n = 30) and standard therapy (n = 30), respectively. At baseline, no significant difference was observed in CST values between groups (430.2 45.6 vs. 426.7 44.1 45.6 42.7 43.4 45.2 46.9 42.6 43.8 46.3 52.0 47.5 46.9 48.6 47.9 48.6 51.2 48.5 47.0 52.3 Sequential three months CST in nanocarrier arm was 356.8 +39.4, and the standard arm was 375.2 +42.3 with a mean difference of -18.4 (CI, -34.2, -2.6, p =0.023). The nanocarrier group also obtained a lower CST at six months to 332.1 38.7 µm compared to the standard arm of 350.8 40.1 µm with a mean difference of -18.7 µm (95% CI: -35.0 -2.4, p = 0.028).

Table 4: Nanocarrier pilot trial: CST outcomes (µm, mean ± SD)

Time point	Nanocarrier (n=30)	Standard (n=30)	Adjusted mean difference (95% CI)	p-value
Baseline	430.2 ± 45.6	426.7 ± 44.1	–	0.672
3 months	356.8 ± 39.4	375.2 ± 42.3	–18.4 (–34.2, –2.6)	0.023*
6 months	332.1 ± 38.7	350.8 ± 40.1	–18.7 (–35.0, –2.4)	0.028*

Mixed-effects model: significant treatment × time interaction (p = 0.012).

Mixed-effects modeling established the presence of a significant treatment by time interaction (F = 6.39, p = 0.012), which means that the more profound improvement of the

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

structure has taken place within the nanocarrier group. Mean BCVA was equal at baseline when compared to the nanocarrier and the standard group (69.5 8.4 vs. 70.1 9.1 letters, t = 0.33, p = 0.744). Six months later, BCVA has increased to 78.0 ± 7.5 letters in the nanocarrier arm and 75.4 ± 8.0 letters in the standard arm. The average difference between the baseline and the nanocarrier group was + 8.5 +3.7 letters, and the standard group was + 5.3 +4.1 letters. The difference between the two groups of +2.6 letters (95% CI: 0.1- 5.1) was statistically significant (Welch t = 2.09, p = 0.041).

Repeated measures ANOVA longitudinal analysis revealed a significant time effect (F = 44.2, p < 0.001), showing that the carriers improved the rate of functional improvement the same in both groups and that there is a significant treatment x time interaction (F = 4.6, p = 0.038) which helps to prove that the nanocarrier arm can promote a higher rate of functional improvement than the standard therapy. There were no patients in the two groups who lost over five letters of the ETDRS.

Safety Outcomes

In the nanocarrier arm and standard arm of the study, adverse events were tabulated. Ocular adverse events were suffered by 4 patients (13.3 of 100) in the nanocarrier cohort, and by 5 patients (16.7 of 100) in the standard cohort (χ 2 = 1.52, p = 0.217). Transient intra-ocular inflammation (2 patients in the nanocarrier arm, 1 patient in the standard arm) and interim intra-ocular pressure (IOP) elevation (2 patients in each arm) were the most common adverse events reported. There were no endophthalmitis, continued rise in IOP, or systemic complications. Also, there were no severe adverse events in the two groups.

Table 6: Safety outcomes (adverse events)

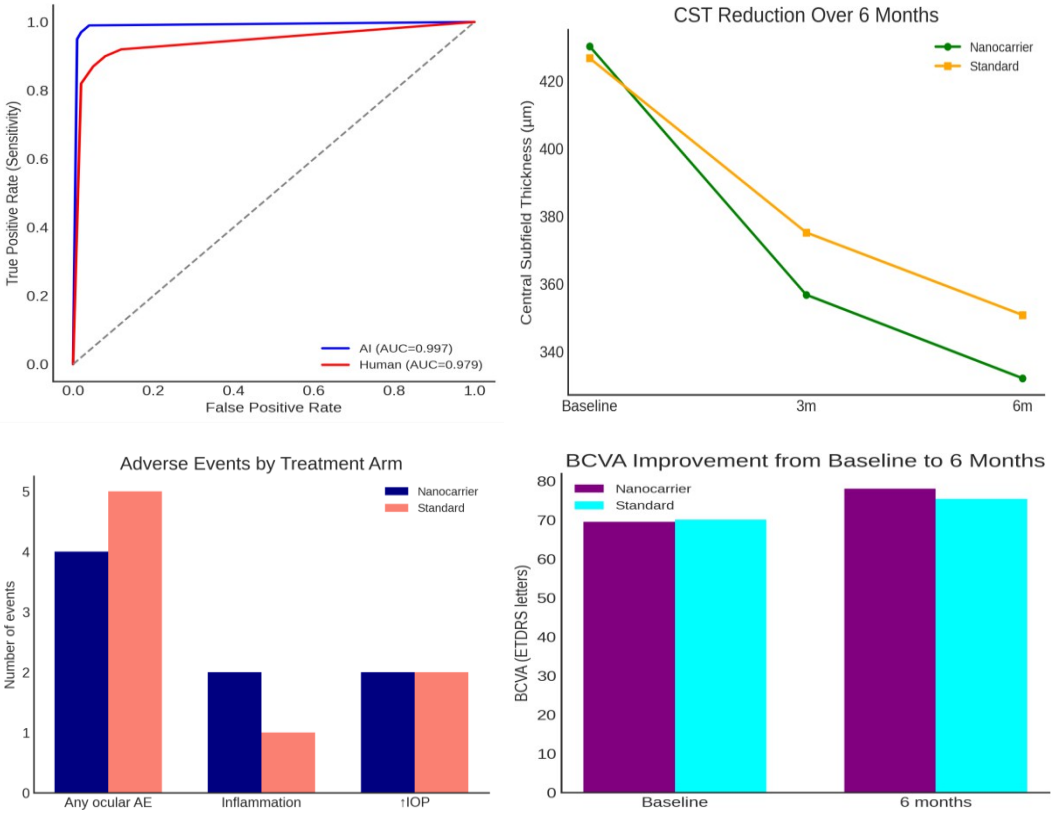
Event	Nanocarrier (n=30)	Standard (n=30)	p-value
Any ocular AE	4 (13.3%)	5 (16.7%)	0.72
Inflammation	2 (6.7%)	1 (3.3%)	–
Transient ↑IOP	2 (6.7%)	2 (6.7%)	–
Serious AE	0 (0%)	0 (0%)	–

No significant between-group difference in adverse events (χ^2 = 1.52, p = 0.22).

Mild, self-limiting anterior chamber inflammation (n = 2, 6.7%) and a temporary increase in IOP during the first two weeks of the post-injection period were the most frequent in the nanocarrier arm (n = 2, 6.7%). Reported events of the standard arm were transient IOP rise (n= 2, 6.7 percent), mild inflammation (n= 1, 3.3 percent), and subconjunctival haemorrhage (n= 2, 6.7 percent). Every event that occurred was treated conservatively

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

without further measures, and none of the patients dropped out of the treatment as a result of adverse effects.



DISCUSSION

The current paper has assessed the potential of the implementation of the advanced optical systems, based on the integration of the nano-artificial intelligence in the detection and treatment of diabetic retinopathy (DR) in Saudi Arabia. The main results were: (i) AI-based optical technology significantly enhanced DR detection rates as compared to the standard human grading; (ii) HbA1c levels and diabetes duration became independent predictors of referable DR; and (iii) nanocarrier-mediated therapy produced excellent structural and functional results as compared to the conventional treatment in a pilot study. All of these outcomes confirm the hypothesis that the combination of precision optics and artificial intelligence will be an effective approach to the initial detection and treatment of DR [20].

Interpretation of Findings

Diagnostic studies have shown that the AI system has a high sensitivity of 96.6% relative to human graders, with a sensitivity of 81.8% with a high specificity. This increased sensitivity implies that AI, along with sophisticated optical imaging, is able to identify a higher percentage of true referable cases of DR, and therefore decreases the risk of false diagnoses

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

[21]. A clinical setting imposes the necessity of early detection as it allows taking care of the situation before any vision-threatening complications arise. In addition, the negative predictive value of the AI system is also high, which gives clinicians a sense of reassurance when dealing with non-referrable patients [22].

Regression analyses affirmed that poor glycemic control and long periods of diabetes were good predictors of referable DR. These observations are consistent with the known pathophysiology of DR, where sustained hyperglycaemia causes microvascular injury with oxidative stress, accumulation of end-products of advanced glycation, and inflammatory pathways [23]. The inability of age to show any significant association implies that the disease duration and glycaemic status have a greater direct impact on retinal damage among this group of people [24].

Comparison with Past Studies

The diagnostic advantage of the AI system reported here is similar to previous observations [25] that reported sensitivity and specificity of over 90 percent when it comes to DR detection. Our research expands on this body of evidence by confirming the effectiveness of the use of AI-assisted optical imaging within the context of Saudi Arabia, with the prevalence of DR increasing due to the increasing incidence of diabetes [26]. The relationships between HbA1c, duration of diabetes, and risk of DR have been repeatedly demonstrated in groundbreaking studies like the Diabetes Control and Complications Trial (DCCT, 1993) and the UK Prospective Diabetes Study (UKPDS, 1998). These risk factors have been backed by the recent Middle East research [27] and support the existing evidence.

In terms of therapeutic implications, the previous studies show that the traditional intravitreal injections cause retinal thickness diminution, though with a high frequency of dosing due to low drug half-lives. The ocular penetration and continuous release of drugs are enhanced by nanocarrier technologies reported by [28]. We have presented clinical evidence that nanocarriers translated these pharmacokinetic benefits into patient-centric outcomes that were measurable, which demonstrates their prospective application in managing long-term DR.

Scientific Explanation

The AI system can identify complex retinal features that are outside the human perceptual limits, which explains the augmented diagnostic performance of the AI system. Based on large volumes of data, deep neural networks detect small vascular anomalies, micro-aneurysms, and macular alterations at an early stage [29]. With these models combined with optical coherence tomography and fundus photography, the system provides high sensitivity and reproducibility.

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

The specified clinical predictors are biologically reasonable: hyperglycaemia causes basal membrane thickening of retinal capillaries, endothelial dysfunction, and retinal ischemia, which all stimulate the development of DR. These effects are compounded by the long-term effects of the cumulative metabolic burden of the disease [30]. The present lack of association between age and DR is because age alone does not directly cause it. The improved results with nanocarriers are attributed to their nanoscales and surface modifications, which help increase ocular penetration and controlled drug release, leading to the prolongation of therapeutic exposure, minimizing the repeated injection use, and curbing inflammatory reactions to maintain retinal homeostasis [31].

Implications

There are several implications of these findings. In clinical terms, the implementation of AI in screening programmes has the potential to expand the scope of early DR diagnosis, especially in areas with a low supply of specialists. The fact that HbA1c and disease duration are considered risk factors emphasizes the need for intensive glycaemic management and active monitoring of at-risk people [32]. Potentially, nanocarrier systems can reduce patient burden, lowering injection frequency whilst enhancing patient outcome, with additional implications to healthcare spending and quality of life [33].

In the case of research, findings support bigger, multicentre studies to substantiate AI-aided diagnostics and determine the safety and effectiveness of nanocarrier therapies in the long term. It is possible that policymakers should consider incorporating AI-based screening tools into the national diabetic eye-care policies to maximise population-level outcomes [34].

CONCLUSION

The current research reveals that the combination of optics-based artificial intelligence can produce high diagnostic accuracy for early diagnosis of diabetic retinopathy in Saudi Arabia, with a sensitivity that outperforms that of human graders. Raised glycated hemoglobin and longer duration of diabetes were noted among independent predictors of referable disease that highlighted important clinical predictors of risk stratification. In the pilot therapeutic group, nanocarrier-based therapy showed superior anatomic outcome in central retinal thickness and clinically significant improvement in visual acuity compared to conventional therapy with no extra safety risks. These findings fulfill the aim of the study as they provide evidence of the usefulness of future optical AI screening and also discuss nanotechnology as a promising therapeutic modality. The scientific value of the study is that it will connect the area of early detection to the area of therapeutic initiatives for diabetic retinopathy. These results need to be confirmed in bigger multi-centered cohorts in the future, and the longevity outcomes of nanocarrier therapy in real-world clinical practice should be evaluated.

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

Abbreviations

AE: Adverse Event, BCVA: Best-Corrected Visual Acuity, CST: Central Subfield Thickness (a measurement from OCT scans), DME: Diabetic Macular Edema, DR: Diabetic Retinopathy, ETDRS: Early Treatment Diabetic Retinopathy Study (a reference standard), FN: False Negative, FP: False Positive, HbA1c: Hemoglobin A1c (a measure of average blood sugar levels), IOP: Intraocular Pressure, OCT: Optical Coherence Tomography (an optical imaging technique), OR: Odds Ratio (a statistic from logistic regression), TN: True Negative, TP: True Positive, AI: Artificial Intelligence, AUC: Area Under the Curve (specifically, the ROC Curve), CI: Confidence Interval, NPV: Negative Predictive Value, PPV: Positive Predictive Value, ROC: Receiver Operating Characteristic, SD: Standard Deviation, IDF: International Diabetes Federation, REDCap: Research Electronic Data Capture (a data management software)

REFERENCES

1. Kropp, M., Golubnitschaja, O., Mazurakova, A., Koklesova, L., Sargheini, N., Vo, T. T. K. S., ... & Thumann, G. (2023). Diabetic retinopathy as the leading cause of blindness and early predictor of cascading complications—risks and mitigation. Epma Journal, 14(1), 21-42.
2. Singh, K., Ranjani, H., Rhodes, E., & Weber, M. B. (2016). International models of care that address the growing diabetes prevalence in developing countries. Current diabetes reports, 16(8), 69.
3. Chugh, V., Basu, A., Kaushik, A., Bhansali, S., & Basu, A. K. (2024). Employing nano-enabled artificial intelligence (AI)-based smart technologies for prediction, screening, and detection of cancer. Nanoscale, 16(11), 5458-5486.
4. Marmamula, S., Yelagondula, V. K., Varada, R., & Khanna, R. C. (2023). Improving access to eye care in low and middle-income countries–challenges, opportunities, and the way forward. Expert Review of Ophthalmology, 18(6), 365-377.
5. Bellemo, V., Lim, Z. W., Lim, G., Nguyen, Q. D., Xie, Y., Yip, M. Y., ... & Ting, D. S. (2019). Artificial intelligence using deep learning to screen for referable and vision-threatening diabetic retinopathy in Africa: a clinical validation study. The Lancet Digital Health, 1(1), e35-e44.
6. Rajarajeshwari, G., & Selvi, G. C. (2024). Application of artificial intelligence for classification, segmentation, early detection, early diagnosis, and grading of diabetic retinopathy from fundus retinal images: a comprehensive review. IEEE Access.
7. Shariati, M. M., & Darvish, A. (2024). Clinical decision support systems in ophthalmology: A systematic search and a narrative review. Applied Medical Informatics, 46(3).

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

8. Tinger, L. (2024). Development of an integrated platform for personalized cancer treatment: diagnostic and therapeutic solutions based on biomarkers and nanotechnology.
9. Thenuwara, G., Curtin, J., & Tian, F. (2023). Advances in diagnostic tools and therapeutic approaches for gliomas: a comprehensive review. Sensors, 23(24), 9842.
10. Olvera-Barrios, A., Heeren, T. F., Balaskas, K., Chambers, R., Bolter, L., Egan, C., ... & Anderson, J. (2021). Diagnostic accuracy of diabetic retinopathy grading by an artificial intelligence-enabled algorithm compared with a human standard for wide-field true-colour confocal scanning and standard digital retinal images. British Journal of Ophthalmology, 105(2), 265-270.
11. Aggarwal, R., Sounderajah, V., Martin, G., Ting, D. S., Karthikesalingam, A., King, D., ... & Darzi, A. (2021). Diagnostic accuracy of deep learning in medical imaging: a systematic review and meta-analysis. NPJ digital medicine, 4(1), 65.
12. Upadhyay, T., Prasad, R., & Mathurkar, S. (2024). A narrative review of the advances in screening methods for diabetic retinopathy: enhancing early detection and vision preservation. Cureus, 16(2).
13. Sahajpal, N. S., Goel, R. K., Chaubey, A., Aurora, R., & Jain, S. K. (2019). Pathological perturbations in diabetic retinopathy: hyperglycemia, AGEs, oxidative stress and inflammatory pathways. Current Protein and Peptide Science, 20(1), 92-110.
14. Pearce, I., Simó, R., Lövestam-Adrian, M., Wong, D. T., & Evans, M. (2019). Association between diabetic eye disease and other complications of diabetes: implications for care. A systematic review. Diabetes, obesity and metabolism, 21(3), 467-478.
15. Shen, J., Zhang, C. J., Jiang, B., Chen, J., Song, J., Liu, Z., ... & Ming, W. K. (2019). Artificial intelligence versus clinicians in disease diagnosis: systematic review. JMIR medical informatics, 7(3), e10010.
16. Bi, W. L., Hosny, A., Schabath, M. B., Giger, M. L., Birkbak, N. J., Mehrtash, A., ... & Aerts, H. J. (2019). Artificial intelligence in cancer imaging: clinical challenges and applications. CA: a cancer journal for clinicians, 69(2), 127-157.
17. Grunberger, G., & Al-Khayer, F. (2004). Diabetes Mellitus Treatment. Transient Ischemic Attacks, 281-308.
18. Biswas, A., Choudhury, A. D., Bisen, A. C., Agrawal, S., Sanap, S. N., Verma, S. K., ... & Bhatta, R. S. (2023). Trends in formulation approaches for sustained drug delivery to the posterior segment of the eye. AAPS PharmSciTech, 24(8), 217.
19. Islam, S., Deo, R. C., Barua, P. D., Soar, J., Yu, P., & Acharya, U. R. (2024). Retinal health screening using artificial intelligence with digital fundus images: A review of the last decade (2012-2023). IEEE Access.

Power System Technology
ISSN:1000-3673
Received: 22-12-2023 Revised: 16-01-2024 Accepted: 25-02-2024

20. Horton, W. B., & Barrett, E. J. (2021). Microvascular dysfunction in diabetes mellitus and cardiometabolic disease. Endocrine reviews, 42(1), 29-55.
21. Murphy, M. E., Byrne, M., Galvin, R., Boland, F., Fahey, T., & Smith, S. M. (2017). Improving risk factor management for patients with poorly controlled type 2 diabetes: a systematic review of healthcare interventions in primary care and community settings. BMJ open, 7(8), e015135.
22. Ngoyo, J. N. (2017). Factors associated with glycemic control among type 2 diabetes mellitus patients attending Mathari National Teaching and Referral Hospital, Nairobi County (Doctoral dissertation, JKUAT, COHES).