BioSpectrum
the business of Bi
24 years of leveraging the business of Bio
www.biospectrumindia.co

AI-Driven Therapeutics for Diabetes

31 October 2023 | Features | By Dr Manbeena Chawla

Diabetes mellitus, a chronic metabolic non-communicable disease (NCD), has attained epidemic proportions worldwide. Several studies conducted over the last two decades have revealed a huge burden of diabetes in India, which translates to a large population of individuals at risk of not only cardiovascular disease but also chronic complications of diabetes such as kidney, foot, and eye disease. The cost of treating them is crippling not just individuals, but also the society and the country as a whole. For instance, diabetic foot ulcers and infections are responsible for more than 30 per cent of hospitalisations related to diabetes mellitus. On the other hand, there is a higher prevalence of diabetic retinopathy among the urban population than in the rural population. India must step up state-specific policies and technological interventions on a war footing to arrest the rapidly rising epidemic of diabetes.



According to the Indian Council of Medical Research (ICMR) study conducted in 2021, India has over 101 million people living with diabetes compared to 70 million people in 2019, with at least 136 million people (15.3 per cent of the population) having prediabetes.

A ground-breaking research paper of a comprehensive epidemiological study funded by ICMR was recently published in the globally acclaimed medical journal, The Lancet Diabetes and Endocrinology, revealing that Goa has the highest prevalence of diabetes while Uttar Pradesh is at the lowest. Likewise, Sikkim has the highest number of cases with prediabetes while Mizoram has the lowest.

Funded by the ICMR and Ministry of Health and Family Welfare, Government of India, the Indian Council of Medical Research–India Diabetes (ICMR-INDIAB) study is the largest survey on diabetes and other metabolic NCDs undertaken in India.

On one hand, this study identifies regional and state-level variations in the prevalence of diabetes across the country. At the same time, on the other hand, it highlights the growing complications due to the rising number of diabetes cases.

“There is a sizeable population in India at risk of long-term organ complications due to metabolic diseases such as diabetes, which are likely to pose a major public health challenge in the near future. There is also evidence that the epidemic is spreading to rural areas, which lack the health infrastructure needed to effectively diagnose and manage these conditions”, says **Dr V Mohan, Chairman, Dr. Mohan’s Diabetes Specialities Centre (DMDSC) and Madras Diabetes Research Foundation (MDRF)**.

The Diabetes Domino Effect

Complications from diabetes can be classified as microvascular which include nervous system damage (neuropathy), renal system damage (nephropathy) and eye damage (retinopathy), diabetic foot ulcers or macrovascular disease that include cardiovascular disease, stroke, and peripheral vascular disease.

Based on a figure of about 40 million people with diabetes in India, there would be at least 7 million with diabetic retinopathy, 0.8 million with diabetic nephropathy, 10.4 million with diabetic neuropathy, 8.5 million with coronary artery disease, and 2.5 million with peripheral vascular disease. The burden due to diabetic complications is very high in India simply because of the large number of people with diabetes.

Data reveals that approximately, 12-15 per cent of people with diabetes suffer from diabetic foot ulcers at least once in a lifetime, and 5-24 per cent of them finally lead to limb amputation within 6-18 months after the first evaluation.

On the whole, diabetic retinopathy and diabetic foot ulcer are the most frequent, and the most disabling complications of diabetes mellitus, with a sinister impact on patients' quality of life. As a result, diabetic retinopathy, one of the first manifestations of microvascular disease, remains today, despite improvements in monitoring and treatment, one of the leading causes of blindness worldwide.

Leveraging AI Technology

In India, the threat of diabetic retinopathy is looming with a recent study showing a 16.9 per cent prevalence. This has led to the call for more innovative approaches to prevent and treat diabetic retinopathy. One promising solution is the use of artificial intelligence (AI) for improved eye care in patients with diabetic retinopathy.

Although, currently there are a few private players in India, both at the industry and academic level, that are utilising AI and related technologies to develop new tools for quick detection of diabetic retinopathy, its complete implementation is still a long way to go.

To name a few, Bengaluru-based companies such as Remidio, and Forus Health are some of the prominent players that are strengthening the use of AI in the timely and effective detection of diabetic retinopathy in India and other parts of the world. Remidio has developed the world's only smartphone-based automated algorithm that works offline. The algorithm harnesses deep learning technology deployed on a smartphone-based fundus camera, Remidio NM-FOP, to detect referable diabetic retinopathy within 10 seconds. The company has recently received CE mark approval for its technology, closely following the nod received from Singapore's Health Sciences Authority (HSA).

"People with diabetes require regular and repetitive annual retinal screening for timely detection of diabetic retinopathy in addition to diabetes assessment. The current utility of AI in diabetic retinopathy is limited to preventive care, that is, in screening, with a rising interest in predictive features toward disease advancement and treatment burden. The integration of AI into healthcare can help in larger coverage for screening for diabetic retinopathy but there are several challenges that stand in the way of wider adoption of AI such as workflow integration, enhanced explainability and interpretability, workforce education, data quality, access, and sharing and compliance with privacy", says **Dr Rajiv Raman, Senior Vitreo-Retinal Consultant, Sankara Nethralaya**.

In a similar vein, **Dr Doris Macharia, Senior Vice President, Global Programmes, Orbis** says, "In India and elsewhere around the world, investment in AI is needed to bridge the gap in eye care management, especially in ways that can make managing diabetic retinopathy cost-effective, easier, and more convenient, eventually reducing vision loss and blindness in the country."

Besides diabetic retinopathy, there's a promising technology to detect diabetic foot ulcer. Pune-based biotech startup Mylab Discovery Solutions has recently partnered with a UK-based firm to develop a kit to detect diabetic foot ulcers. It is one of the world's first point-of-decision molecular technology solutions, delivering early identification of the spectrum of microbial flora in the ulcer and supporting clinicians to plan appropriate antimicrobial therapy regimes.

Another complication that arises from diabetes is nerve damage. One in ten people and one in two diabetics suffer from Peripheral Neuropathy, a chronic clinical condition, wherein the peripheral nervous system is damaged.

Various epidemiological studies from India have shown the wide prevalence of nerve damage varying from 5 to 2400 per 10,000 population. The prevalence of nerve damage in India is estimated to vary between 13.1 and 45 per cent in different populations which could be attributed to different types of diabetes.

Highlighting the technological advancements in this space, researchers at the Department of Mechanical Engineering, Indian Institute of Science (IISc), Bengaluru in collaboration with the Karnataka Institute of Endocrinology and Research (KIER), have developed a set of unique self-regulating footwear utilising 3D printing technology.

The footwear can be especially beneficial for people who have diabetic peripheral neuropathy. The researchers have currently collaborated with Bengaluru-based startups Foot Secure and Yostra Labs to commercialise this product.

Another example is of Mumbai-based startup Ayati Devices, in collaboration with the Indian Institute of Technology (IIT) Bombay, which has developed a quick screening tool to quantify the severity of foot neuropathy. The product has been approved by the Central Drugs Standard Control Organisation (CDSCO).

Addressing Complications Effectively

With insulin and oral anti-diabetic drugs holding the major interest of the Indian pharma sector, there are very few companies that are investing in developing specific solutions for diabetes-related complications. The market for oral antidiabetic drugs is fragmented whereas the market for insulin is concentrated in nature with top players dominating the majority of the industry. The volume of new entrants in the patented oral antidiabetics and insulin market is low, while in the generic oral antidiabetics market it is comparatively higher.

“Insulin is the bedrock of diabetes treatment. It turns a deadly disease into a manageable one for 9 million people with type 1 diabetes. For people living with type 2 diabetes, insulin is essential in reducing the risk of kidney failure, blindness and limb amputation. However, one out of every two people needing insulin does not get it because of a number of factors including high prices”, points out **Dr Kiran Mazumdar Shaw, Executive Chairperson, Biocon**.

Addressing diabetes-related complications, Asprius Lifesciences, a Gujarat-based pharmaceutical company, has developed a new treatment for diabetic neuropathy. The company has already filed a patent for its innovative fixed-dose combination drug.

Focusing on another diabetes-related complication, diabetic nephropathy or complication related to the kidneys, Bayer recently launched its drug Finerenone to treat chronic kidney disease associated with type-2 diabetes in India. The drug will be sold under the brand name Kerendia in India.

Mumbai-based pharmaceutical firm Alkem Laboratories is exploring the use of 4D bioprinting technology in collaboration with a South Korean company to treat the deep, non-healing, chronic wounds associated with diabetic foot ulcers. Likewise, Bengaluru-based Stempeutics Research, a group company of Manipal Education and Medical Group, is currently undergoing phase 3 clinical trials for its innovative product to treat non-healing diabetic foot ulcers. The company has out-licensed the product to pharmaceutical firm Cipla for exclusive marketing rights for five years in India.

According to **Dr Pawan Gupta, Senior Vice President, Medical and Regulatory Affairs, Stempeutics**, “Current standard of care for treating non-healing diabetic ulcer includes local wound care with sterile dressings, repeated debridement of necrotic tissues, and pressure off-loading. However, most results are far from satisfactory, and about 20 per cent of patients with diabetic foot ulcers undergo limb amputation. Since DFU is a complex clinical condition, current approaches endeavour to address one single approach, which leads to the failure of complete healing. Cell therapy-based approaches have several advantages compared to others, as they allow therapeutic targeting of different phases of wound healing.”

Also, Mumbai-based Centaur Pharma has already launched a new chemical entity (NCE)- based product for the treatment of diabetic foot ulcers in the Indian market, in collaboration with German company Cyto Tools.

Entod Pharma is another player from Mumbai that has recently developed a saffron-based eye care supplement to treat and manage diabetic retinopathy, along with other eye-related diseases.

Diagnose, Identify, Treat

Although the Union Health Ministry has launched an ambitious initiative of screening and putting 75 million people with hypertension and diabetes on standard care by 2025, equal attention is needed to diagnose, identify and treat the organ complications that arise due to diabetes in an economical way.

Currently, there is a dearth of economic evidence about screening programmes, affected age groups, and frequency of screening for diabetes and related diseases in Indian settings.

“Right intervention to delay the onset of diabetes and the related complications is key. The public health centres should engage more with the industry players that are developing multiple diabetes management apps in order to educate, raise awareness and increase communication about prediabetes, diabetes and the related complications. Health education and the engagement of people with diabetes about the related complications such as diabetic retinopathy, the risk it poses to their vision and the need for annual retinal examination, are essential and should be made mandatory”, says **Dr Uma Nambiar, international healthcare consultant**.

Sharing his perspective, **Dr Anand Sivaraman, Founding Director and Chief Executive Officer, Remidio** says, “There is an urgent need to make the diagnosis of diabetes and complications such as diabetic retinopathy accessible and affordable, particularly at primary care centres, using technology like AI and portable imaging systems that can be used by nurses and

health workers. For instance, UK NHS's Diabetic Eye Screening Programme in GP offices was able to eliminate Diabetic Eye Disease as a cause of blindness in working-age adults, through early detection. The programme commenced in 2003 and reached population coverage across the whole of England by 2008. The benefit of the programme is that, in the UK, diabetic retinopathy is no longer the leading cause of certifiable blindness in the working age group."

In fact, the government of Kerala is trying to replicate the same model with Remidio's device with deployment in more than 150 primary health centres.

Dr Jitendra Singh, Union Minister of Science and Technology who is also a renowned diabetologist and Professor, is optimistic that India is ready to lead technology-driven diabetes care. But he insists that results would be better following public-private partnerships.

"There is a pressing need for more innovative programmes and institutions for non-communicable diseases, particularly diabetes. The necessity of dedicated diabetes institutions for research and training will lead to ultimately contributing to better healthcare and well-being for all. It is therefore the right time to generate as much Indian data as possible because the goal should be to develop Indian treatment regimens for Indian patients, and Indian solutions for Indian problems. And this would be possible with effective collaboration between the public and private sector", the Minister emphasised.

We hope to see more investments and engagements from both the public and private sectors in India in newer technologies and areas to detect diabetes and related complications more accurately and economically in the years to come.

Dr Manbeena Chawla

(manbeena.chawla@mmactiv.com)