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Exclusive: Does India need a Precision Medicine Initiative?

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During his State of the Union address in January 2015 at the White House in Washington DC, American President Mr Barack Obama announced the launch of the most ambitious Healthcare initiative called the Precision Medicine Initiative (PMI), a mission to usher the US into a new era of medicine where patients will enjoy individualized and tailor-made treatments for various ailments.

Mr Obama said, "Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type - that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"

Too Early For India?

Precision medicine is an emerging approach of medicine which looks at the root cause of an illness, rather than addressing the symptoms alone. Precision medicine may not be very well known as Personalized Medicine. But they are one and the same. It takes into account individual variability in genes, environment, and lifestyle for each person. The need and its potential in the Indian Healthcare scenario is high, considering that the system is under great pressure due to sheer numbers.

Precision Medicine in the country is considered to be at an early adoption stage. A diverse country like India, with over 4000 population groups, and a significant percentage of consanguineous marriages presents a high-risk and prevalence of inherited genetic disorders that require attention for early diagnosis, right treatment, and management. India has a heavy burden of inherited diseases driven by the unique genetic characteristics in the population. With 1.4 billion people, the absolute number of patients suffering from diseases in which genetics play a role is significantly large.

It is reported that Indians witness a loss of around $23 billion from their annual income in treating or getting tested for non-communicable diseases.

The global Genomics industry is predicted to grow at around 18% in the next 10 years, and India is expected to be a major

stakeholder. Revenue growth in molecular diagnostics in 2013 was reported to be around 15%. Clinical diagnostics in one of the fastest growing fields which may cross $2 billion by 2018. Preventive healthcare is growing at the rate of 25%, which will boost Healthcare revenues and the country's Precision Medicine scenario.

"Genetic testing is slowly getting acceptance among our clinicians. The challenges are about creating the awareness for wide-spread adoption. It is not at all too early for the country to embrace precision medicine. This is primarily because India is an emerging market for genomics. A rising middle-class, state-of-art healthcare facilities and expert physicians are driving the growth of the industry in India.... I expect the industry to attain double digit growth," says Mr Sam Santhosh, Chairman & Global CEO, MedGenome.

Dr Saleem Mohammed, CEO & Founder, Xcode Life Sciences, agrees that India has a strong need for Precision Medicine which will significantly reduce its Healthcare burden.

"It is estimated that only around 40% of the medicines we take are effective and appropriate for us. Today, we practice trial-and-error medicine which does not consider in detail the person-to-person variability, which is a key source of variation for the effectiveness of drugs. You can imagine being dosed and prescribed by taking into account various factors such as age, gender, genetics, medical conditions and usage of other drugs. That is the promise of personalized medicine, and India needs to take leadership in this domain," he adds.

In India, Precision Medicine is being practiced in several specialties like oncology, cardiology, psychiatry and diabetology. It is already being embraced in India to a reasonable extent, especially in cancer.

"Each individual is an island, and so now that the molecular complexity of disease has been deciphered, the role of genetics, environment and epigenetics are clearly telling us that that we all need to receive treatment designed for our physiology and body type," remarks Dr Villoo Morawala-Patell, Founder & CMD, Avesthagen.

Indian Healthcare institutions are fast adopting technologies that can make them on par with the best in the world. The need to modernize, and be on par with global standards can be seen amongst large hospitals and private medical institutions.

Explains Dr Kalyanasundaram Subramanian, CSO, Strand Life Sciences, "There are several targeted therapies that work only on patients who have a specific genotype or genomic variation. So, patients are tested before the therapy is prescribed. Cancer is probably the disease in which precision medicine is most advanced. However, there are several other diseases - cardiac, ophthalmic, and certain types of diabetes, where knowing the genetic background of the disease can help with disease management. Here the field is not as advanced."

Like most technologies, India is expected to be a follower-market in Precision Medicine. Doctors would like approval from USFDA or the American Medical Association (AMA) for it to become mainstream in their practice.

But the challenge is that the West is going to fund studies in Caucasian population and not the Indian. In fact, most drugs are designed and manufactured for Caucasian population. Unless India accelerates research in this space, validation in the Indian context will always be questionable.

"Precision medicine is badly needed to move towards personalized medicine and personalized diagnostics, which has a huge potential to reduce the burden of national healthcare costs," points Dr Amit Kumar, CEO & CSO, BioAxis DNA Research Centre. "At several instances, this results in patients selling assets or borrowing money to pay incurring medical expenses. Precision medicine is the best available tool and remedy for combating this huge economic burden."

Cost of these tests are a concern still, given India is largely a self-paid economy. But as technologies improve, the cost of sequencing is seen to reduce.

Precision Medicine offers a possible answer by reducing the costs of hospice stay, and reducing the overall financial, physical and psychological costs of the try-and-test approach of medicine.

"The infrastructure needed for precision medicine is taking shape in India. There are certain issues to be addressed for it to gain the needed momentum," opines Mr Samarth, CEO & Founder, Positive Bioscience.

"The key is also the analysis of genomics data, which as we automate will provide higher efficiency in the entire data analysis process, thereby making tests more affordable. We do need more baseline genomics data of Indian origin which will help us in refining our analysis on clinical cases in the country," comments Mr Sam.

Targeted therapies like Imatinib have been around for 40 years. This has changed the prognosis of Chronic Myeloid

Leukemia (CML) in children.

"People used to think that the role of genetics ended with hereditary disease. Today we know that every response our body makes has a genetic fingerprint to it. We can now predict response to different therapies, and thus avoid trial-and-error medicine which is both costly, time-consuming, and puts an unnecessary drug and hospitalization burden on the patient," comments Dr Sooraj Ratnakumar, Founder & Scientist, Swagene.

The US and EU markets do have a head start in Personalized Medicine in terms of accessibility to resources and raw materials, government funding, and regulations.

"There is also greater awareness among the people there about the benefits of personalized medicine. In India, we have an excellent gene pool of biotech and IT professionals. With government interest, we can easily build India as the hub of personalized medicine," expresses Ms Anu Acharya, CEO, Mapmygenome.

President, CEO & Founder of Genotypic Technology Mr Raja Mugasimangalam says that Precision Medicine is too early for India at the moment. "Precision medicine is an emerging field and sufficient success should be shown by the western world for India to embrace it. It is in its early phase, and there is not sufficient government support in the form of research grants in this space," he adds.

Overly Hyped?

The way Precision Medicine can help transform Healthcare, especially treatment and management of deadly non-communicable diseases is tremendous, and stalwarts opine that it is not an overly hyped concept.

"The field of precision medicine is still in a nascent stage in India, and much needs to be done to create awareness. So the concept cannot be called as overly hyped, but rather passionately acclaimed in the medical and scientific fraternity. Any development in the science and medical space that revolutionizes how medicine will be practiced in the future naturally generates a buzz around it. Yes, the concept is quite novel at this point of time but its scope is tremendous. While we may lack the bandwidth to carry out all the exceptional research at this point in time, slowly it will happen. And once it happens, the impact will be more than just overwhelming. However, there are certain roadblocks that we cannot ignore. But limitations and challenge begets innovation and development," opines Mr Samarth.

"I see precision medicine as a new hope rather than a hype," Dr Amit states. "Some of our clients say that research insights of the genomics data-related to lifestyle, diet, and clinical methods have been very useful in making a decision faster based on a patient's personalized genetic information."

More than hype, Precision Medicine is said to be more of plain, pure common sense. For thousands of years, humans have known that there is inter-individual variability when it comes to things ingested, be it medicine or food. Why then patients pop an over-the-counter pill? Or even wonder whether it will work on them or not?

In a recent study by Johns Hopkins University (USA), medical error was suspected to be the third leading cause of death in the US. Many of them are related to improper drugs and improper drug dosages.

"It's sort of like 'death by medicine'. Can you imagine what the statistics are in India? asks Dr Saleem. "Today, we don't question why the outcome was negative for a patient. We assume that the medical establishment did the best they can in good faith. With increasing prevalence of clinical decision support systems, and insurance insisting on good practices, you will see things improve. Common sense dictates that precision medicine is the only way medicine should be practiced and not by trial-and-error."

Dr Binay Panda, Chief Officer & Head, Ganit Labs, also states that the problem in India is that Precision Medicine is hyped by people who understand little about it.

"Look around and you will find folks who talk about precision medicine, who understand little about it or have very little practical and scientific experience on developing precision medicine tests. We need rigorous scientific minds to talk about the utility of precision medicine, like in the west, and not those who use the term as a buzz word or a part of marketing supplements only," clarifies Dr Binay.

India's Research Scene

The research scene for Precision Medicine in India is largely in the beginning stage. Some studies are being carried out in various translational research centres across the country.

There are several Government laboratories such as IGIB (Institute of Genomics & Integrative Biology), CCMB (Centre for Cellular and Molecular Biology), hospitals such as CMC Vellore, LV Prasad Eye Institute and other organizations, where research is being conducted. "However, it would be fair to say that the research is fragmented and individual researcher-driven, and not yet translated to patient care in a big way," points Dr Kalyanasundaram.

Research is also being carried out at Sir Gangaram Hospital (Delhi), Madras Diabetes Research Foundation (MDRF) (Chennai), Indian Council of Medical Research (ICMR), Institute of Bioinformatics (IOB) (Bangalore), and Government institutions such as National Institute of Biomedical Genomics (NIBMG) and Center for Genome Research.

Large Government hospitals like Tata Memorial Hospital, National Institute of Mental Health and Neurosciences (NIMHANS), and All India Institute of Medical Sciences (AIIMS) are also involved in the identification of new disease genes and biomarkers by applying Genomics.

Dr Mallik Sundaram, Co-founder, President & CEO, Mitra Biotech, says, "The western markets have embraced it quickly because healthcare is more organized there with the payers being the government or insurance companies, thereby translating the benefits of decreased healthcare costs while improving treatment success rates using precision medicine. In countries like India with fragmented healthcare, and the patient frequently being the payer, while the benefits remain the same, but acknowledging and translating them is more piecemeal."

India, like many other developing countries, is following success stories of the West.

"Success in precision medicine depends on several factors including availability of tests on precision medicine, system on which medical payment is made -- out-of-pocket versus insurance-based versus government-sponsored -- overall positive atmosphere in the country towards embracing new tests, previous success stories, availability of skilled manpower and the presence of the right environment. On all these accounts, we in India, have miles to go. However, we have excellence in pockets, which include brilliant people who are capable of doing all that. The trick is to encourage those few to develop tests for the Indian population," Dr Binay explains.

Paradoxical Elements

The use of Precision Medicine is a little tricky and paradoxical, say experts.

"It has lot of social impact. But someone has to draw a line to the extent one should use it. One single mutation is responsible for more than one medical condition and vice versa; it may also create confusions and misleading interpretations. Precision medicine may be only a corroborative aspect until we have more confidence, and accurate outcomes getting reported across the globe," Dr Amit reveals.

Dr Kalyanasundaram says that the challenge is in marrying personalization of medicine with reduced drug costs to an individual patient.

"Currently, most of the best genome-based medicines are expensive and out-of-reach for the average Indian. The other worrying aspect is that none of these medicines are available in India. Imagine the plight of a patient who realizes that there are medicines that may work for him but is unable to access it," he observes.

Also, the discussion of paradoxes of Precision Medicine often revolves around the cost, i.e., spending more and more to identify therapies that applies to fewer and fewer.

Mr Samarth adds, "This paradox can be compared to the cost of any IT initiative in the eighties era using mainframe computers, and specially created buildings for housing them versus, even higher computational processing being available today in a mobile system; or 3D printing to give a more recent example. As there is a change in approach and increase in use of the technologies, there will be a reduction in costs."

What Is Needed?

In Precision Medicine, for successful commercialization, many things have to come together.

"There has to be a way of leveraging all the information and insights that is generated in other populations from around the

world. The Indian government should be setting up large genomic studies in various disease populations. Indian scientific establishments needs to view this as a challenge, and work with physicians to understand the diseases that are most likely to have benefits quickly, and work towards problems in those areas. Indian funding agencies should be funding large translational projects with a clear clinical aim. There should be clear frameworks that allow industry to access these insights to convert them to products," urges Dr Kalyanasundaram.

Both Mr Sam and Mr Samarth agree that increasing the awareness levels of Precision Medicine among the general population, clinicians and doctors is much needed.

"In our country, the depth and width of the healthcare system is very large, often unorganized, and under tremendous pressure. To bring in a new approach to the practice of medicine will need full participation and education of patients, drug developing pharma companies in pharmacogenomics, change in the practices and process of hospitals and clinics, good regulatory framework and the support of the government in building the research infrastructure. Further in order to translate the bench research to bedside care, it is important for research academics and medical market players join hands," suggests Mr Samarth.

Collaboration of genetic testing laboratories, hospitals, and medical doctors may be the starting point, says Dr Amit. "We require huge genetic, clinical and lifestyle data from India, and this can only be reached if governmental programs backup such kind of association and research. With the fast decreasing cost of DNA sequencing of a person's genome, a model shall be framed which should have genetic medicine and precision therapy as one of the most important inclusion. Government may think of including genetic tests under the insurance coverage, starting with critical illnesses. If we have enough country data, it may offer a lot of very important medical insights."

According to Dr Binay, India needs 4 Ps to make Precision Medicine succeed. "They are people, processes, protocols and pricing. People meaning encouraging and aiding brilliant minds to be involved in developing new and innovative tests; processes meaning developing the right clinical and scientific processes or SOPs; protocols meaning coming up with the right regulatory...," he lists.

Dr Saleem believes that the medical community should actively collaborate with genetic service providers to validate concepts in the Indian population.

"We operate in a highly cost-sensitive environment. A key barrier to adoption is cost of the test.... In the long-term, genetics should become a major part of the medical curriculum. Genetics should get its due importance given that we live in an era where we are talking about actively editing genes to cure major diseases," he notes.

Mr Sam recommends public-private partnerships (PPP) between academic institutes and the industry to promote genomic research in the country.

"Partnerships with private enterprises that have already taken the leap into genomics research and are providing solutions to address health care needs in India.... In addition to this, initiatives like setting up of electronic medical records, and population level genome sequencing will go a long way in helping commercial success. It will also be useful to chart out a comprehensive plan to identify key disease areas in India with underlying genetic reasons that have high unmet medical need and to allocate government funds to promote education, research and innovation in these areas," he stresses.

Should India Ape The US?

India may follow something similar to PMI launched by Mr Obama, but on a pilot scale.

"The government can play a key role by allocating research funding to this area. Precision medicine is going to have a tremendous impact on our nation's healthcare and will improve health outcomes while minimizing the costs. But someone has to make the investment in accelerating the creation of know-how, and the knowledge base that is specific to India. Given the significance of health for a nation's economic and social development, I would say that prioritizing of government grant funding to this area will be highly useful. The US again has taken leadership in this so far with the precision medicine under the Obamacare," voices Mr Samarth.

In an interview with BioSpectrum, Dr Mandar Kulkarni, CTO, Cancer Genetics India, states, "I think this is a big challenge even in the US, where most diagnostic testing is paid through insurance reimbursements, which are driven by FDA-approvals."

He further expresses, "Currently, the FDA is reviewing the guidelines and ensuring that the testing is not wasteful. On the other hand, a major advantage for such testing in the US is the availability of well-curated databases that define the effect of

mutations on the disease-state in terms of prognosis, clinical outcome and treatment options. Unless we adopt the tests and begin this exercise, we will not be able to identify epidemiological and etiological differences that contribute to cancer in India."

Though India's limited studies in this area show that while the Indian genome has many similarities to the Caucasian, there are significant differences as well. "So it is absolutely essential that a similar and large PMI be launched in India given the genomic diversity here," justifies Dr Kalyanasundaram.

Mr Sam also agrees that a initiative like PMI will be useful to India's Healthcare. "If a similar program is initiated, it has to be designed keeping in mind the state of the economy, and the public health issues of the Indian population, and the diseases or disorders plaguing our society. The GenomeAsia 100K consortium is one such initiative in the region," he urges.

Starting anything new is good, but India needs to revive and encourage what it already has, and have a long-term vision for Personalized Medicine.

"Science does not bear fruit overnight," Dr Binay adds. "One needs to be patient and encourage funding the right talent in this direction. First and foremost, we need to encourage young minds to pursue science and be more meritocratic in our institutions."

Dr Amit emphasizes that both ICMR (Indian Council of Medical Research) and CSIR (Council of Scientific and Industrial Research) need to play a very important role in framing the insights related to pharmacogenomics, genetic variation-related drug studies, and population-wise human SNP validation, if India wants a meaningful outcomes from such a diverse population.

Dr Raja says that India doesn't have to ape the West.

One might consider a PMI in India as an overly zealous move for a country where malnutrition and poverty collectively kills more people than diseases.

"At the right time we can definitely think of taking a step towards PMI for our own country just like America. India is already the diabetes capital of the world and is slowly inching in vying the top spot for heart ailments and cancer too. I think we all have come to appreciate the fact that all these diseases are genetic-driven by a combination of several mutations in different genes. Precision medicine guided by genomics not only allows us to diagnose and prevent these diseases but also treat and manage them effectively," elaborates Mr Samarth.

Regulatory Woes

Genomic information is critical since it not only affects an individual but potentially their family as well. There are legal, technical, social, and political hurdles which needs to be addressed.

Dr Kalyanasundaram stresses, "It needs to be clear who owns this information, what are the limitations under which researchers get access to it, and how can this information be used and misused. These issues are all critical and need to be addressed by the law."

However, the current regulatory frameworks are inadequate in terms of providing guidelines for Precision Medicine initiatives.

Information is required on how to bring in a population level-approach for Genomics research. Also, policy revisions to support the industry from import duties on reagents are a need of the hour.

"Intellectual property rights and patent policies are not very well defined in the area of precision medicine and predictive genomics. This could be a challenge to further innovation. Also, reimbursement from insurance companies is another key factor that will determine the growth of this industry. In the western world, insurers have started accepting genomic tests in their formulary as it is expected to reduce the cost of down-the-line treatment. In India the option is to bring the test at affordable prices and foster innovation to reduce the cost of genomic diagnosis," Mr Sam expresses.

Precision Medicine is dependent on the DNA Study of an Individual, and India does not have a DNA usage policy yet.

"We are hoping for the best since this important master molecule has caught the attention of our PM Narendra Modi, and he has announced to put all the efforts towards the DNA Bill of India. Again, draft of this Bill also needs to be concreted by including insights from industry experts, academicians, research organizations, laboratories and judiciaries," justifies Dr Amit.

Dr Binay strongly supports in having strong ethical guidelines to practice Precision Medicine.

Degree Of Impact

Just imagine a patient taking a simple blood or saliva test at a laboratory, and in the next meeting his or her physician is very well prepared with the patient's genetic horoscope including the information on chemical compounds, or combination of drugs useful or harmful to him, based on the tried-and-tested genetic test report.

"We will be able to minimize side effects with very beautiful and faster accurate therapies that too at affordable costs if precision medicine boosts up in India..... If used responsibly, it can do wonders and contribute towards every individual's good health," notes Dr Amit.

Precision Medicine can also transform the national economy, especially in a population whose average lifespan is increasing.

Mr Sam explains, "From an individual's perspective, it has the potential to make genetic diagnosis of diseases more efficient and cost-effective, by reducing genetic testing to a single analysis, which informs individuals throughout their life. Since it uses state-of-the-art genomic technologies, rich medical record data, tissue and blood banks, and clinical knowledge that will allow clinicians and payers to tailor treatments to individuals, it can greatly reduce costs of ineffective therapies incurred through the current trial-and-error clinical paradigm."

The impact can be great, where patients get the right medications, have better outcomes and lower side effects, feels Dr Kalyanasundaram. "This would lead to healthier populations with better overall health economics. To make this possible, lots of information needs to be collected, analyzed and translated. Medicines that can exploit the genetic differences need to be present. So the task is formidable but the payoffs are potentially enormous."

Precision Medicine will also allow reduced morbidity, specifically in oncology cases, help in preventing high burden of genetic diseases, and managing high-risk cases with increased surveillance. It will also have a major impact on the economy by reducing productivity losses, and decreasing costs of treating disease, thereby reducing overall costs on Indian Healthcare.

"The internet will further accelerate adoption of precision medicine by empowering patients and doctors who are already demanding more to fight India's unique challenges with diabetes, heart disease and tobacco use," said Dr Sooraj.

In 2012, Futures Group predicted a new perspective to Healthcare by 2050, where gaps between medical practice, healthcare, and personal health will be bridged.

Another prediction is the predominance of preventive healthcare, where individuals take charge of their health by harnessing the power of technology. Genomic tests - single nucleotide polymorphism and whole genome sequencing - will be the key catalysts to this change.

"We have seen the beginning of this change. Wellness was once a fancy word. Today, it is part of every hospital's business strategy to engage a new generation of customers, who are actively pursuing wellness using social apps for various reasons - right from fitness and diet to finding the best doctor," opines Ms Anu.

In India, diseases have a profound physical, psychological and social impact. Most of healthcare costs are paid not out of insurance, but out of pockets.

The impact of illness in one person in the family has a domino effect on the family and the community. "The cost of treatment, for diseases like cancer, cardiac diseases, diabetes, asthma, and the impact of the side effects of medication taken has often seen families, even amongst middle-class and higher middle-class, needing to take loans, or family members having to leave jobs," Mr Samarth states. "Just the simple factor of reducing treatment time and side effects will have a significant impact on the socio-economic situation of an individual."

So, diseases that were previously a death sentence will be manageable, or even curable, because we will be able to individualize therapy for each patient.