OPINION

Diagnosis and treatment of genome at the gamete and embryo levels: the probable future of major diseases

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Four major diseases, namely cancer, cardiovascular disease, diabetes and infertility have been severely affecting the global human population. The World Health Organization has taken special initiatives to control these diseases by 2030. Since these diseases are closely related to genetic causes, it is highly essential to treat the root cause(s) or the source which is at the point of genesis. Here we hypothesize a strategy to prevent and treat such diseases at the levels of gamete and embryo, which will enable us to control them at their source. In the wake of the 2019 coronavirus pandemic, identification of genes related to the defence mechanism against the virus in the recovered patients seems of utmost importance and may prove useful in future prevention and treatment.

The human embryo is formed by the fusion of a sperm and an oocyte, which thereby inherits genetic information in a compact form without any phenotypic expression. This event further results in the recombination of genes which may be beneficial or harmful to the host human body. There are well-known clinical genetic syndromes and diseases such as Down's syndrome, haemophilia and thalassemia; however, there are few studies in respect to those genetic sequences which may remain dormant without any symptoms but may get activated later due to some other cause(s) affecting active human lifespan.

It has been estimated that cancer and cardiovascular disease (CVD) are the leading causes of death in the world[1]. In addition, two non-communicable diseases, namely diabetes and infertility also severely affect the global population. In view of the constantly increasing incidence of these diseases, the United Nations under its Sustainable Development Goals 2018 has targeted the reduction of premature mortality from such non-communicable diseases by one-third by 2030, through prevention and treatment. To achieve this goal, it seems extremely essential to evolve a fool-proof strategy to identify the causes well in advance in order to check the genesis or source of such diseases.

Statement of the hypothesis

It is evident that the root cause of major communicable and non-communicable diseases is largely linked to the genes and DNA. We hypothesize a future scientific strategy to counter the possibility of these gene-associated disorders and diseases by identification and treatment at the level of the gene and embryo.

Supporting evidence for the hypothesis

Cancer

Cancer is caused by the abnormal or uncontrolled proliferation of a cell in any organ, which may be due to any of the following factors:

- Exposure to mutagen(s)/carcinogen(s).
- Failure in the repair of the damaged DNA.
- Activation of oncogene(s).
- Lack of tumour suppressor gene(s).
- Lack of DNA repair gene(s).
- Failure of apoptosis.

The close relationship of cancer with the genes and DNA has been supported by a number of studies[2–6]. These scientific evidences strongly indicate that the basal cause(s) of genesis of cancer have a genetic association, which can be affected by other factors such as environment, diet and family history.

Cardiovascular disease

CVD is one of the major causes of global human mortality. The World Health Organization (WHO) estimated an annual loss of 17.9 million lives in 2015 due to CVDs[7]. Scientists have been making efforts to specifically identify the genetic causes and several studies have provided evidence for the genetic linkage of CVD, which is possibly heritable[8–11]. However, the clinical manifestation may be influenced by other known factors.

Diabetes

According to an estimation by the International Diabetes Federation, the number of people affected with diabetes may increase up to 522 million by 2030 (ref. 12). Several genetic mutations are highly associated with the risk of diabetes; however, treatments are available after the disease is diagnosed and are purely aimed at the symptoms rather than the cause[13–15].

Infertility

It has been estimated that around 48.5 million couples worldwide are affected by infertility[16]. However, the prevalence estimates for lifetime infertility vary widely in different regions because of the lack of a common consensus[17]. It is reported that one in every four couples in developing countries is affected by infertility[16]. There may be variability in the prevalence, but it is apparent that the problem is global.

The causal factors have been categorized as: (a) female factors; (b) male factors; (c) both male and female factors, and (d) unexplained causes. The incidence of these causes is highly variable due to many reasons. The largest category being 'unexplained causes' indicates some genetic association. Extensive scientific reviews in this respect have identified and stressed on the importance of genes for human infertility[18–22]. However, there is still a great need for collaborative studies on large cohorts to ascertain the causes of this multi-factorial disease.

Evaluation and consequences of the hypothesis

The four major non-communicable diseases discussed here severely affect human populations all over the world and are closely linked with DNA and genes. Therefore, the control of these diseases seems to be at the point of genesis. Although the genetic mechanism is much complicated and is affected by several co-factor elimination of these diseases may be possible by the following proposed strategy:

(1) Identification of wanted and unwanted genes on a global collaborative basis to develop a gene library.
(2) Identification of individuals/populations carrying the unwanted gene(s).
(3) Developing *in vitro* and animal models for research on inactivation of the unwanted gene(s) at the gamete and embryo level.
(4) Safe and effective gene therapy at gamete and embryo levels to control/replace the unwanted gene(s) in the affected individuals.

The effective outcome of this scientific strategy can also be of great value for the 2019 novel coronavirus (SARS-CoV-2) pandemic. Globally the number of new infections is constantly rising, but simultaneously there is high percentage of recovered patients. The important questions that need to be answered are: Why did not all the infected patients die of the virus? why have some patients recovered with minimal symptoms? The answer seems to be related to the genetic defensive mechanism of the recovered as well as uninfected exposed patients which protected them from the primary and secondary consequences of this deadly virus. In view of these facts, the future treatment of communicable as well as non-communicable diseases may be possible by gene therapy and advanced genomic medicine.

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