Epigenetic Alterations and their Impact on Assisted Reproduction Technology Outcomes

It is already three decades since the birth of the first "test-tube baby" in 1978 and such methods have found their due place in most countries. In Denmark alone, more than 6% of children are born through assisted reproduction technologies (ARTs) (1).

In the United States, more than 50,000 babies are born through IVF annually and there are more than 4 million people born through such methods around the world (2).

In the beginning, there were much opposition and criticism surrounding the use of these methods, which mostly consisted of criticisms about gamete manipulation and the induction of genetic and chromsomal disorders in embryos (2). By extensive use of these methods and the birth, growth and puberty of these children, criticisms and concerns abated and the marriage and successful pregnancy of Louise Brown dampened disputes about the fertility of these children.

Recently, following the rise in the number of babies born through ART and statistical evaluation on the health of IVF children, there have been reports on the increasing number of abortion, intrauterine fetal death, congenital anomalies and abnormal epigenetic modifications in these children (3). Although most of the causes of these problems are not understood exactly, but epigenetic alterations in the gametes and embryos are believed to be the potential causes (4).

Studies have shown the evidences of gametes epigenetic alterations during gametogenesis and these changes seem to be essential for the natural fertilization, quality and development of embryos, fate of pregnancy and health of the offspring during his life. These changes include covalent changes such as methylation, phosphorylation, acetylation, etc at DNA level or in proteins (histones and protamines) attached to it without any changes in the sequence of DNA nucleotides affecting the developmental process and function of every cell, tissue, organ and organism (4).

Patterns of epigenetic modification could be influenced by environmental conditions and health status of organisms, therefore, assisted reproductive procedures including ovulation induction protocols, fertilization, embryo culture conditions and physico-chemical environment of IVF labs could influence the epigenetic modifications of gametes, embryos and even the fetus. In addition, one of the hot topics in ART and management of IVF centers are intensive care through quality control (QC) and quality assurance (QA) for all the materials, methods, instruments and procedures (5).

Taking these points into account, it seems that most of the indices used for the assessment of ART methods including the rate of fertilization and the number and quality of embryos need to be revised in the near future. Although certain changes in therapeutic protocols may not have obvious effects on ART indexes (due to genomic inactivate of early embryos), but due to epigenetic changes and subsequently gene expression patterns, it may drastically affect the implantation rate, pregnancy outcomes and health status of IVF children. This will not be possible unless we design studies to identify the conditions with minimal alterations from normal epigenetic patterns and subsequently maintain these conditions in IVF centers through rigorous implementation of QC and QA. Presently, these topics are hot subjects of papers and lectures in the field of reproduction and infertility and future studies would emphasize on the detection of normal epigenetic modifications and their abnormal aberrations throughout ART procedures and their potential effects on embryos and IVF children. In conclusion, this scenario will lead to obvious changes in the infertility treatment protocols to provide more safety and success rate with lower costs.

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