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Editorial Open access

Reproductive Genetics

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Editorial

Genetics has a role in every discipline of medicine. Traditionally it is known that genetic disorders are untreatable hence hesitation to invest on genetic disease. Now this concept is changing. The major contribution of genetics is to predict and prevent a disorder thus decreasing its burden right from the planning of reproduction. To fulfil this objective a new branch, known as Reproductive Genetics, has immerged. Reproductive genetics is a branch of science that deals with the genetic contribution of reproductive process, both natural and assisted. Now it expands to include studying genetic as well as epigenetic modifications of genome and its effect on reproduction. Genetic factors are greatly responsible for infertility, abortion, stillbirth, malformation and cancer. Reproductive genetics is becoming an integral part of today's reproductive practice due to increase in the burden of reproductive disorders. The ideal time to apply reproductive genetics should be from the time of pre-conception or peri-conception period so that prediction and/or prevention (primary and/or secondary) is possible. Advances in molecular and reproductive technology (next generation sequencing and microarray), introduction of non-invasive prenatal screening/testing (NIPS/NIPT), preimplantation genetic screening/diagnosis (PGD/PGS), rapid prenatal diagnosis, fetal imaging (fetal ultrasonography/fetal MRI), etc. has increased this drive and expectations of public. The NIPT/NIPS is an upcoming technology for screening fetal aneuploidies (in particular trisomy 21) from cell-free fetal DNA (cffDNA) present in blood of pregnant woman. The low false positive rate is the most important advantage of NIPT as it allows women to avoid unnecessary invasive procedures such as amniocentesis or chorionic villous sampling (trisomy 21 pick-up rate as high as 1 in 2; far better than 1 in 250 with serum screening like triple/dual marker tests). The NIPT/NIPS can also determine paternity, fetal sex, fetal rhesus D (RhD) status, copy number variations (microdeletion/microduplication syndromes) or even single gene disorders but not yet recommended by professional bodies. The advent of preimplantation and prenatal diagnosis has allowed option of having unaffected offspring in couples at risk of transmitting genetic disorder. Preimplantation genetic screening using DNA microarray/NGS improves the effectiveness of *in vitro* fertilization by selecting normal embryo for implantation. This has immensely increased the scope of genetic testing in reproductive practice. Moreover, progress has been made in universal screening to detect abnormal fetuses. This has further extended the need for reproductive genetics. Furthermore, rapid dissemination of information to public and health care provider has affected daily reproductive care so much that an understanding of genetics is essential for all reproductive specialist in particular to know risk of a genetic disorder and how to prevent. This knowledge will protect reproductive specialist from medico-legal consequences following failing in preventing genetic disorders in a family. Reproductive disorders requiring expert management from a reproductive genetics specialist are unexplained repeated pregnancy loss (e.g., abortion, intrauterine deaths, hydrops, hydramnios, preeclampsia, growth retardation, hydatidiform mole, etc.), fetal malformation (particularly recurrent), unexplained infertility, recurrent failure of assisted reproduction, premature ovarian failure, polycystic ovarian syndrome, unexplained primary amenorrhoea, endometriosis, azoospermia/oligospermia, disorder of sex development, advanced parental age, abnormal maternal serum screening test, abnormal obstetric ultrasound evaluation, previous fetus/child with genetic disorder or chromosomal disorder or malformations, parent with genetic disorder, family history of genetic disorder, maternal disorders associated with an increased risk for fetal congenital defect (e.g., maternal diabetes, epilepsy on epileptics, etc.), maternal exposure to teratogen (drugs, infections, radiation, toxins, etc.) in peri-conception period, consanguinity, before and after offering prenatal/preimplantation screening or prenatal/preimplantation diagnosis, familial reproductive cancer, risk to reproduction from cancer chemotherapy/radiotherapy and risk to offspring from cancer chemotherapy/radiotherapy, etc. [1].

The infertility is another major area in reproductive genetics. Genetics (mostly of sex chromosomes) account for 15–30% of male and 10-15% of female infertility as of now but this are going to change in the near future as many newer genetic/genomic/epigenomic factors are coming [1]. The genetic basis of infertility may result from chromosomal abnormalities, Yq microdeletion, CNVs (particularly sex chromosomes), monogenic, multifactorial, epigenomic, mitochondrial, etc. We have observed CNVs in pseudo autosomal regions 1 and 2 (PAR 1 and 2) as well as gain (3 copies) in AZF loci besides global/specific (e.g., GSTT1 gene) hypomethylation in testicular maturation arrest [2]. The other well-known genetic defects/ mutations associated with male infertility are CFTR (vassal agenesis)/CATSPER1 (asthenozoospermia)/SPATA16 and DPY19L2 (globozoospermia)/AURKC (macro spermatozoa) and with female infertility are FMR1/FOXL2/BMP15 genes. Genetics is becoming more important following the development of *in vitro* fertilization and intra cytoplasmic sperm injection as these procedures lead to more genetic abnormality in offspring, since it passess through *in vitro* system as well as bypasses physiological protective mechanisms. Available data so far have shown that there is an increased risk of chromosomal abnormality, in particular sex chromosome, congenital malformations and imprinting defects in babies conceived by ART/ICSI besides epigenetic effects (including birth weight) related to *in vitro* culture, cryopreservation, handling stress, etc.

An understanding of reproductive genetics of major developmental disorders is also important for today's perinatal care specialists [3]. Detailed assessment of malformed fetus after termination of pregnancy (spontaneous/induced) is important for precise diagnosis. The challenges are to understand pathophysiology of lethal developmental

defects and to resolute phenotype and genotype heterogeneity. It is hoped that the information generated on this field in coming years and later integrated in system biology will be of great service to answer questions that are encountered every day in teratology/dysmorphology practice viz., genetic/genomic role, underlying pathophysiology, early prediction or prevention and feasibility of pharmacotherapy.

Advances in reproductive technology like cellular reprogramming or cellular differentiation/ dedifferentiation, etc. has created another dimension for reproductive genetics. Now, in the laboratory stem cell can be manipulated to become specialized cells and can be used to treat disease. Embryonic stem cells can be differentiated into gamete (sperm/oocytes) to treat infertility or into trophoblast for studying human placental development and function. Therefore, development of novel method for precisely controlled differentiation is crucial to facilitate the application in clinical practice or research. Recent progress in germline stem cell isolation and culture may provide a platform for *in vitro* gamete development and may open a new era of gametogenesis in a dish and personalized infertility treatment in coming years. For therapy with stem cells, the issue of immunocompatibility arises. The breakthroughs in somatic cell nuclear transfer have raised the possibility of generating unlimited sources of undifferentiated cells, with potential applications (therapeutic/reproductive cloning) without immune rejection.

Another area of reproductive genetics is reproductive cancers which needs special attention as reproductive cancers are increasing, appearing in very younger age (in particular ovarian; 35% cases below 25 years), poor prognosis due to late diagnosis (ovarian epithelial cancer), following exposure (estrogen) in fetal life (testicular dysgenesis syndrome, adenocarcinoma uterus/vagina, etc.) and often familial (breast, ovary, endometrium). Germ line mutations are responsible for familial cancer viz., BRCA mutation in familial breast and ovarian cancer. In the current era of genome sequencing, clinical cancer diagnosis is undergoing a transformation [4]. This technology has enabled the discovery of genes implicated in cancer risk and creating opportunities for the development of more precise and early tumor detection, even at preimplantation/prenatal stage. The growing possibility of cancer prediction, prevention and early precision treatment seems reality.

Once genomic screening technologies are used as part of predictive medicine practice, high-risk groups may be identified before development of disease and appropriate measures may be started before the pathology is too late in near future. Cases like klinefelter syndrome, turner syndrome, Yq microdeletion, premature ovarian failure, etc where pathology manifests after puberty may benefit in future through predictive genomic medicine practice (prediction before disease manifestation followed by preventive measures like gonad/gamete cryopreservation and later when required *in vitro/in vivo* gametogenesis).

References

1. Halder A (2015) Reproductive Genetic Counselling in Genomic Era. EC Gynaecology 2 : 132-148.
2. Halder A, Jain M, Kumar P (2015) Primary Testicular Failure: An Overview. J Clin Diagn Res 3: e105.
3. Halder A (2014) Lethal Developmental Defects: An Overview. Open Journal of Obstetrics and Gynecology 4: 1006-1036.
4. Halder A (2015) Canceromics and P3 medicine. J Clin Diagn Res 3: e104.