ORIGINAL ARTICLE

Pre-natal genetic counseling in a resource limited country — a single center geneticist's perspectives

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Abstract

Objective: To assess the needs related to prenatal genetic counselling in a developing country.

Methods: The prospective observational study was conducted at the Prenatal-Genetic Counselling Clinic of Aga Khan University Hospital, Karachi, from October 2007 to September 2010. In-depth interviews were conducted and the data was stored in the form of patient charts. Information was then extracted from the charts and entered into a structured questionnaire.

Results: Of the 93 couples in the study, 49(53%) were in the self-referral group and 44(47%) were in the physician-referral group. Diagnosis was not given for previously affected children by the paediatrician or by obstetrician for recurrent miscarriages in 68(73%)cases. Besides, 20(22%) couples had voluntarily terminated a pregnancy without any tests because of the fear of having a diseased child. Eleven (12%) couples were looking for amniocentensis or chorionic villus sampling. Death in previous children was the main reason to seek genetic counselling and was seen in 57(61%) couples. Consanguinity was seen in 77(83%) couples.

Conclusion: A clear deficiency of knowledge of genetics was seen among the non-genetic healthcare providers. Demand of antenatal genetic testing among the public was also seen, highlighting the need of diagnostic facility for genetic and metabolic disorders. However, this needs to be explored in the context of the existing healthcare infrastructure.

Keywords: Prenatal genetic counselling, Prenatal genetic testing, Consanguinity, Genetic disorders, Pakistan. (JPMA 64: 1008; 2014)

Introduction

Every year an estimated 8 million children — 6 per cent of all live-births worldwide — are born with a serious birth defect of genetic or partially genetic origin.[1] Congenital anomalies account for 3% of deaths in all children under five years of age.[2] Families with an individual with genetic disorder have a much higher probability of having a child with birth defect. Such families often seek prenatal genetic counselling (PGC).

Genetic counselling (GC) is defined by the National Society of Genetic Counsellors as a process of helping people "to understand and adapt to the medical, psychological and familial implication of genetic contribution to disease".[3] PGC deals with questions about genetic risk factors for the offspring.

GC has two core elements; an accurate diagnosis in proband and recurrence risk calculation based on the mode of inheritance for the disease in question. With the advancement in prenatal diagnosis many congenital malformations, chromosome disorders and metabolic disorders are detected during early pregnancy. However, in a substantial proportion of families at risk for genetic disorders "probability counselling" still remains the only option.[4]

Families seeking GC are looking for answers to the four questions; what is the problem, how did this happen, is it a treatable condition and will this recur in future pregnancies. Genetic counsellor or geneticist can answer these questions with certainty only if an accurate diagnosis has been established in the family. In Pakistan, GC is a very young field. The current study provides important insights into PGC issues and the needs in a developing country like Pakistan.

Subjects and Methods

The retrospective observational study was conducted at the Aga Khan University Hospital (AKUH), Karachi. The patient population at the hospital represents a diversity of ethnicities in the country. About 61 per cent of all marriages in Pakistan are consanguineous,[5] and a major contributor to both early and late morbidity and mortality.[6,7] Beta-thalassemia is reported as the most common autosomal recessive disorder in Pakistani population.[8] In this backdrop, a PGC clinic was established by the AKUH Department of Paediatrics and Child Health

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in October 2007. Housed with a trained staff geneticist, it is the only nationwide institute providing formal PGC to couples. The centre was established with the aim of providing comprehensive and evidence-based GC relying on the information available for the disease or issues causing concern for the affected families.

The study is basically a chart review of couples who presented to the clinic from October 2007 to September 2010 seeking GC. Potential parents were either referred by self or the family physician. In-depth interviews were conducted, and questions were asked regarding the type and reason of referral, consanguinity and pregnancy history. The data was entered into patient charts. Information was then extracted from the charts and entered into a structured questionnaire after approval from Institutional Ethical Review Committee. Being an exploratory study, only frequencies and percentages were calculated.

Results

A total of 93 couples presented to the PGC clinic over the study period. Of them, 49(53%) couples were self-referred, while 44(47%) were referred by physicians. Majority of physician referrals were by obstetricians 32(73%), while the remaining were paediatricians 12(27%). Among the couples, 40(43%) had received no preliminary counselling of any sort. These couples did not understand the objective of the referral. They had consulted their primary

Table-1: Reasons for which genetic counselling was sought (n=68).

Reasons	No. (%)
Non-specific reasons	19 (28%)
Mental retardation /Developmental delays	16 (24%)
Congenital malformations	8 (12%)
Skeletal dysplasia & carniosynostosis	7 (10%)
Myopathies, muscular dystrophies	7 (10%)
Recurrent hydrops foetalis	6 (9%)
Recurrent miscarriages	5 (7%)

Table-2: Confirmed and clinical diagnoses for which genetic counselling was sought (n=25).

Confirmed Diagnoses	**18 (72%)**
Beta thalassemia minor†	4 (16%)
Cystic fibrosis*	3 (12%)
Balanced translocation	3 (12%)
Fragile-X syndrome*	2 (8%)
Sensorineural Hearing Impairment†	2 (8%)
Isovalericacidemia**	1 (4%)
GlutaricAciduria Type 1**	1 (4%)
Merosin negative muscular dystrophy*	1 (4%)
Panhypopituitrism†	1 (4%)
Clinical Diagnoses	**7 (28%)**
Inborn error of metabolism	3(12%)
Bardet-beidl syndrome	2 (8%)
Intestinal obstruction	1 (4%)
Bladder outlet obstruction	1 (4%)

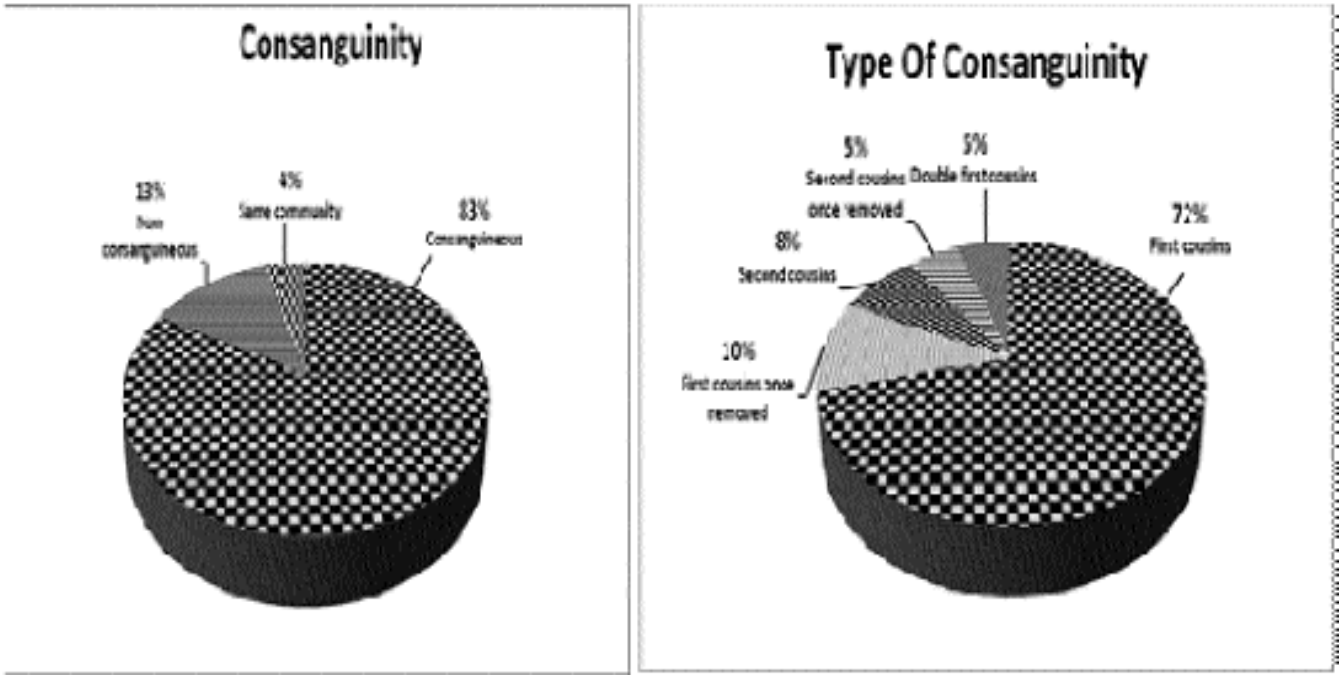

Figure: Consanguinity break-up.

physician with the expectation of getting a cure for their current or future foetus of the medical problem prevailing in their family. Besides, 48(52%) couples presented after conception, and 45(48%) were seen before pregnancy. In the pre-pregnancy group 3(6.66%) couples or their parents sought pre-marital GC.

Overall, 68(73%) couples did not have a diagnosis for their previously affected children or for recurrent miscarriages, and presented with a variety of problems (Table-1). The remaining 25(27%) couples had been given a diagnosis by their respective physicians, which was only clinical for 7(28%) couples, and based on laboratory investigations for 18(72%) (Table-2).

Among the subjects, 20(22%) couples had voluntarily terminated a pregnancy because of the fear of carrying a baby who may have similar problems like their previous children. The main reason leading to prenatal GC was death of previous children as 57(61%) couples had lost children who were suspected to have a genetic disorder.

Eleven (12%) couples wished to have amniocentesis or chorionic villous sampling (CVS). None of these couples had received any counselling regarding amniocentesis and CVS being mere procedures to get foetal deoxyribonucleic acid (DNA) from trophoblast or amniocytes. They were unaware of the fact that although CVS and amniocentesis procedures can be performed by some obstetrician, but only very limited prenatal molecular and cytogenetic testing is available locally.

A large portion of the cohort seen at the pre-natal genetic clinic was consanguineous; 77(83%) compared to 12(13%) who were non-consanguineous. Four (4.3%) couples denied consanguinity but belonged to the same community. First-cousin marriage was the most common type of consanguinity encountered in 55(72%) cases, followed by first cousins once removed in 8(10%), second cousins in 6(8%) and double first cousins in 4(4.3%) and second cousins once removed in 4(4.3%) of couples (Figure).

Discussion

The current study is novel in nature reporting a formal experience of GC in Pakistan and highlighting several points.

More couples sought PGC themselves than after referral by physicians. This may reflect a lack of knowledge among healthcare providers regarding availability of the services or reflective of in-effective collaboration between main referral sources; the obstetricians, paediatricians and geneticists.

Less than half of the couples did not know what to expect from the session. Before starting a counselling session, assessment of consultant's expectations helps in tailoring the counselling according to client's satisfaction and decreases their level of anxiety.[9] If the clients do not know what to expect from GC and they are not given a chance to consider how it may benefit them, there is little opportunity for them to formulate appropriate expectations.[10] Most couples were expecting from the genetic clinic a "cure" of the medical problem prevailing in their family. They expected to get a treatment for the mother-to-be in the form of some oral medicines or injectables, which will prevent the recurrence of the medical problem in their future child. As prenatal genetic testing was not possible in the absence of a definitive genetic diagnosis or "treatment" for neither mother nor foetus could be offered, they were mostly disappointed at not achieving the prime objective.

In this cohort, half of the couples were seen during pregnancy. Two-thirds had not received a diagnosis from the paediatrician for their previously affected children or the obstetrician for repeated miscarriages. Neither the referring physician nor the couple understood the concept of PGC which can be particularly challenging when a pregnancy is already in place.[11] Genetic testing often requires significant amount of time, which is often not available when pregnancy is already there. If a genetic diagnosis is not established in an index case beforehand, prenatal genetic diagnosis is very difficult. Furthermore, if pregnancy is already on-going then the couple does not have alternative reproductive option of pre-implantation genetic diagnosis. GC during pregnancy causes huge concern and anxiety for the family and critical decisions are made under a lot of pressure.

Twelve per cent of the couples asked for an amniocentesis or a CVS to find their foetus genetic status without a diagnosis in their previous children. Couples had considered amniocentesis and CVS as some kind of genetic test which will not only detect the condition in their foetus but will also treat the foetus, thus preventing recurrence of the genetic disorder prevailing in their family. They were very disappointed to learn that there are some 5000 inherited monogeneic diseases which results from mutation involving single gene[12] and more than 500 known metabolic disorders.[13] The lack of awareness among couples seeking care is a reflection of poor information imparted to them by their primary physicians, showing clear deficiencies of knowledge of genetics in non-geneticist healthcare providers.[14]

A striking finding of this study was the high level of acceptance for voluntary termination of pregnancy (TOP) for not only untreatable conditions, but even for disorders

with some physical impairment like achondroplasia or haemophilia, which was seen irrespective of the cultural or educational background. This may be due to their anxiety and fear of having another child with problems as their previous child, and poor availability of multi-disciplinary support system locally that is needed for such disorders.

Despite the fact that 83% of the cohort was consanguineous, it was not the reason to seek GC unlike Iran, where 80% of the couples seek GC mainly for that very reason.[15] In this study primary reason of seeking GC was the death of previous children who were suspected to have some genetic disorder. It is established that already having a sick or disabled child enhances awareness and worry about possible familial genetic risk factor.[16,17] This concern is even higher in a country like Pakistan where there are little treatment options available for treatable metabolic disorders and non-existence of the support system needed for complex genetic and metabolic disorders.

The study has a significant limitation as it cannot comment on the difference in characteristics of patients who sought GC versus those who did not seek such care. Factors like socio-cultural difference, fear of stigmatisation, families' understanding and perception of genetic disorders and their financial resources to seek GC may be different from our study population and may be worth exploring.

Conclusion

The single-centre study signifies some imperative facts. Due to the high level of consanguinity among couples seeking GC, there is a huge risk of genetic diseases in the population. There is a considerable demand for GC services in the country. Given the nature and infrastructure of healthcare in Pakistan, achieving countrywide access to genetic services, including GC, is not conceivable in the near future. Paediatricians and obstetricians may play a vital role in fulfilling this gap between the need and availability of counselling services. Education regarding basic genetics and genetic counselling needs to be built into the training curriculum of these professionals. There is an overlap in the symptoms of genetic illnesses, necessitating correct diagnosis in proband for identification and subsequent prenatal testing. This can be achieved only if sophisticated infrastructure for diagnosis of genetic and metabolic disorders is available. Considering the high costs of services, more international-national partnerships and external funding is required to help those in need of these services.

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