ORIGINAL ARTICLE

ASSOCIATION OF CONSANGUINITY WITH RECURRENT FOETAL LOSS

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Background: Approximately 25% of all recognized pregnancies result in foetal loss. Women who will experience two consecutive foetal loss is less than 5%, while loss of three or more consecutive pregnancies in the first trimester, termed as Recurrent foetal loss (RFL), occurs in 1% of all pregnancies. RFL is often associated with cousin marriages. Keeping in view the social and psychological burden associated with RFL, it deems necessary to conduct further studies, to clear this ambiguity about the adverse effect of consanguinity on the foetal loss. The study was done with the objective to ascertain association of consanguinity with recurrent foetal loss. **Methods:** A total of 432 individual were recruited in this case control study (216 each in case and control groups) and was conducted at the Armed Forces Institute of Pathology (AFIP) Rawalpindi. The Cases consist of women having recurrent foetal loss while controls were women who do not experience recurrent foetal loss. **Results:** The Cases had mean parity level of 5.13 while controls 4.02. The difference in parity level of both cases and controls was statistically significant. The mean live births for all the participants were 2.35±1.915 ranging from 0–7. The cases had 0.72 mean live births while controls had 3.98 mean live births. The cases and controls were compared for consanguinity, i.e., if they had a blood relationship with their husbands. 67 (31.01%) of the cases had consanguinity while 62 (28.70%) of the controls had consanguinity. There was no statistically significant difference among cases and controls in terms of consanguinity. **Conclusion:** Although our study does not show any significant harmful effect of consanguinity on foetal outcome, however more in-depth research is required to look for genetic loci which are contributing to the causation of RFL, especially those inherited recessively, since homozygosity is increased in consanguinity.

Keywords: Recurrent Foetal Loss; Consanguinity; Foetal Loss; Abortion

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INTRODUCTION

Loss of three or more consecutive pregnancies in the first trimester is termed as Recurrent foetal loss (RFL).[1] Foetal loss or abortion is considered quiet common complication of pregnancy yet the prevalence is not greater than 1% of all the pregnencies.[2] Considering the prevalent figures it seems to be a rare issue, however if we see it in context of the psychological and social burden that the families have to bear then we can say that it effects the population significantly.

Although approximately 25% of all recognized pregnancies result in foetal loss, women who will experience two consecutive foetal loss is less than 5%, and 1% for those experiencing three or more foetal losses. The major portion of the pregnancies is lost before a pregnancy is clinically recognizable that is before missed menstrual bleeding. After a positive pregnancy test, 15% of pregnancies are usually miscarry. The percentage of conceptions that result in live birth is around 50%.[3] whether the recurrent miscarriage is a clinical entity or not can be supported by two strands of evidence. Firstly, the frequency of RFL is significantly higher (0.35%) than that expected by chance alone and secondly, in case of a foetal loss in past, the risk of future foetal loss increases. In around 50% of cases the clinical phenomenon cannot be explained. The observed incidence of recurrent foetal loss (0.5–1.0%) is greater than the calculated risk (0.35%), based on a 15% miscarriage risk.[3,4] Therefore, it can be inferred that a subgroup of patients, may have higher risk of foetal loss.

When a woman has three consecutive foetal loses it makes a case for evaluation for RFL, in case of woman of 30–35 years the workup is recommended after two foetal losses.

Many factors are involved in the viability and development of the foetus and an alteration in any of these may result in pregnancy loss. Sometimes more than 1 etiologic factor can cause recurrent foetal loss. The most common causes of recurrent miscarriages are Genetic[5], Immunologic[6], Anatomic[7], Infectious, Environmental causes including alcohol, Caffeine and smoking, Endocrine [8]or Hematologic disorders[9].

All these causes have been investigated in detail in various studies, yet there is another cause that may also contribute to this incident and that is effect of consanguineous marriage. The effect of consanguinity on public health has been studied widely[10], as it is an important social phenomenon and provide financial and emotional security to the families. In our study we aim to

determine the frequency of consanguinity and to find out its effect on recurrent foetal loss. Consanguinity is a matrimonial relationship among individuals having a blood relation with at least one ancestor common among them. The Geneticists classify consanguineous marriage according to the coefficient of consanguinity, defined by the probability that a consanguineous individual has at a given locus, two identical alleles.[11]

Consanguineous marriages are in practice since the existence of mankind. The frequency of such marriages varies as per the population size, extent of isolation, and is influenced by the social, cultural and economic factors.[12] Worldwide, about 20% of the populations live in societies which can be termed as consanguineous.[13] Consanguineous marriages are practiced in Pakistan in almost all areas and social classes. In most parts of Pakistan cousin marriages and specially among the first cousins is preferred and is a common social norm of the society.

As marriage is a basic phenomenon that decides gene redistributions among individuals and over the generations, so as a result of consanguineous marriage there is significant reduction of inter- and intra-population genetic variability. Thus, the degree of homozygosity both at the level of individuals and population increases resulting into an increase in the frequency of abnormalities by fixation of deleterious genes.[14] The effects of consanguineous marriages on, mortality, morbidity and fertility, remained a matter of great interest among researchers, health care providers and geneticists. A vast number of publications are available since the end of the 20th century highlighting this phenomenon.

MATERIAL AND METHODS

This is a case control study conducted in the Armed Forces Institute of Pathology (AFIP) Rawalpindi A total of 432 individual were recruited in the study (216 each in case and control groups). The patients reporting in AFIP from different centres for the work up of RFL were included in the study by purposive sampling. Those having more than 3 foetal losses were recruited and their history was taken regarding foetal loss, family history, marriage history and other sociodemographic variables ethical approval was obtained from AFIP Rawalpindi. The Cases consist of women having recurrent foetal loss whereas controls were women who do not experience recurrent foetal loss. General profile of the study population is given below and briefed in table 1.

Study participants mean age was 28.88±4.59 years ranging from 21 to 44 years. In cases the mean age was 29.12±4.54 while in controls it was 28.64±4.48 years. The educational status of the study subjects showed that 111 (25.69 %) of them had no education at all, while 94 (21.75%) had schooling up to primary level, 104 (24.07%) had middle, 104 (24.07%) college and 19 (4.39%) had university level of education. The same pattern of schooling was seen in both the cases and controls. Majority of the study subjects, i.e., 303 (70.13%) were housewives while 110 (25.46%) office workers and 19(4.39%) were self-employed. The study participants living in urban areas were 279 (64.58%) while the rest 153 (35.42%) were residing in rural areas.

The socioeconomic status of the participants showed that 289 (66.89%) were from middle class, while 70 (16.20%) and 73 (16.89%) were from upper and lower class, respectively. The education level, profession, residence and socioeconomic status in cases and controls followed the same pattern as of the total sample as shown in the table 1.

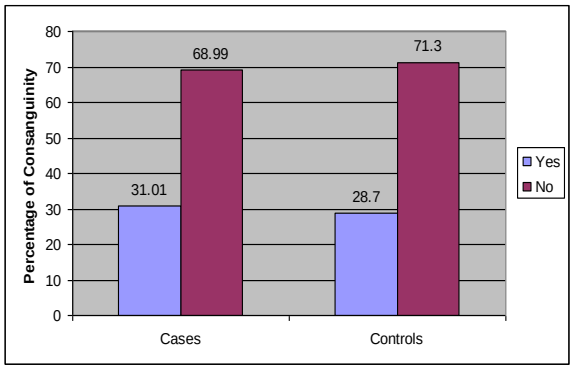

Figure-1: Graph showing comparison between consanguinity of cases and controls.

Table-1: Basic Characteristic of both the Cases and Controls

Characteristic		Cases (%)	Controls (%)	*p*-value
Age (Mean±SD)		29.12±4.54	28.64±4.48	0.264
Education level	No Education	61 (28.2)	50 (23.1)	0.454
	Primary	49 (22.7)	45 (20.8)	
	Middle	45 (20.8)	59 (27.3)	
	College	53 (24.5)	51 (23.6)	
	University	8 (3.7)	11 (5.1)	
Occupation	Housewife	158 (73.1)	145 (67.1)	0.302
	Office Work	48 (22.2)	62 (28.7)	
	Self employed	10 (4.6)	9 (4.2)	
Residence	Urban	143 (66.2)	136 (63)	0.546
	Rural	73 (33.8)	80 (37)	
Socio- economic status	Upper Class	37 (17.1)	33 (15.3)	0.102
	Middle Class	135 (62.5)	154 (71.3)	
	Lower Class	44 (20.4)	29 (13.4)	

Table-2: Comparison of parity in cases and controls

Parity	Cases (%)	Controls (%)	*p*-value
1–4	108 (50)	153 (70.8)	0.000
5–9	108 (50)	63 (29.2)	

Table-3: Comparison of Live birth groups in cases and controls

Live births	Cases (%)	Controls (%)	*p*-value
0	115 (53.2)	0 (0)	0.000
1–3	98 (45.4)	74 (34.3)	
More then 3	3 (1.4)	142 (65.7)	

Table-4: Frequency of first and second-degree consanguinity

	case	Control
First cousins	57 (85.07%)	55 (88.70%)
Second cousin or other relation	10 (14.93%)	7 (11.30%)

The parity status of the participants showed that on average each participant had 4.58 parities ranging from 2–13. Cases had mean parity level of 5.13 while controls 4.02. The difference in parity level of both cases and controls was statistically significant.

The parity was further grouped into two, those having1-4 parities and 5–9 parities and both the groups in cases and controls were compared as shown in table 2. Half of the cases had 1–4 parities while the other half had 5–9 parities. In controls 153(70.8%) had 1–4 parities while 63 (29.2%) had 5–9 parities. The difference in parity level of both the groups was statistically significant.

The mean live births for all the participants were 2.35±1.915 ranging from 0–7. The cases had 0.72 mean live births while controls had 3.98 mean live births.

The live births were further grouped into 3 having no live births, 1–3 and more than 3 live births. The three groups in cases and controls were compared. 115 (53.2%) of the cases had 0 live births while none of controls had 0 live births. 98 (45.4%) of the cases had 1–3 live births while 3 (1.4%) had more than 3 live births. In controls 74 (34.3%) had 1–3 live births and 142 (65.7%) had more than 3 live births. The difference in live births among cases and controls was statistically significant as shown in Table-3

The mean of the number of abortions in the study subjects was 2.10±2.42. The minimum number of abortions was 0 and maximum were 13. In cases the mean number of abortions was 4.20 while there was no abortion in any of the controls.

The cases and controls were compared for consanguinity, i.e., if they had a blood relationship with their husbands. 67 (31.01%) of the cases had consanguinity while 62 (28.70%) of the controls had consanguinity. There was no statistically significant difference among cases and controls in terms of consanguinity as shown in Figure-1

Those participants having positive consanguinity were further analysed for the type of relationship. In cases 57 (85.07%) were first cousin of their husbands while 10 (14.93%) had relationship other than first cousin. In controls 55 (88.70%) were first cousins and 7 (11.30%) had relationship other than first cousin (table 4). Table 4 shows the rate of first-degree consanguine and second- degree consanguine(inbreeding) and it shows 85.07% are first cousin and 14.93% are second cousin or have other relation in cases. Whereas 88.70% are first cousin and 11.30% are second cousin or have other relation in control.

The results do not show any significant effect of consanguinity on abortion in our study population. In cases the abortion rate is slightly higher among consanguineous couples 4.20% compared to non-consanguineous couples 4.09% which is not statistically significant. Whereas in controls there are 0% abortions in both consanguineous as well as nonconsanguineous couple.

DISCUSSION

Varying reports are available in the literature, on the effect of consanguinity on pregnancy outcome, and sometimes variation exists even in the same population group. The rate of consanguinity among Pakistani population is 29.86%. Mostly people opt for consanguineous marriage as a tradition which results in high level of consanguinity detected in our population. The social structure of our region is such that many families are united by social, cultural and economic factors that force them to live in close proximity. The phenomena of such marriages are rare in European countries (<0.5%). More commonly it is practiced in the Muslim world. Comparisons shows that Pakistani population have less frequencies of consanguinity as compared to other Muslim countries. It is less than Kuwait (64.30%)[15] Jordan (63.7%)[16] and Oman 56.3%[17] while it is almost same as that of Palestine (27.70%)[18] and is more than that of Morocco (19.90%)[19].

Diverse data is available on relationship between consanguinity and recurrent foetal loss, some

studies showed a greater prevalence of RFL in consanguineous marriage, while others couldn't prove any association. This study compared consanguinity in RFL cases and controls along with some other factors. The results showed that consanguinity is not a deciding factor for the survival of the offspring. This is in consistence with some other studies such as a cross-sectional study by ISA, A.R on 469 couples with foetal loss in which 237 (50.53%) had consanguineous marriage and 232 (49.47%) had non consanguineous marriage.[20]

In another study obstetrical outcome of 92 Qatari women in a consanguineous marriage having a history of 3 or more early pregnancy losses were compared with 92 non-consanguineous women from the same population and with the same obstetrical history and also matched in maternal age. This retrospective study showed no difference in the rate of previous pregnancy loss and maternal disorders, whereas the prospective study showed no difference in the median gestational age and foetal weight at delivery in ongoing pregnancies or any difference in the rate of subsequent foetal loss.[21]

A study conducted in Kuwait in1980s in, showed higher foetal loss in consanguineous marriages (14.2%) as compared to nonconsanguineous marriages (13.97%), but it is not a statistically significant difference.[22] Another study conducted on Turkish population from 1970–1988, shows an increase prevalence of miscarriage in consanguineous marriages as compared to nonconsanguineous pregnencies.[23]

A study in India reported a strong and statistically significant association between miscarriages and consanguinity. [24] Studies have reported increased prevalence of miscarriages in cousin marriages among Egyptian[25]and Tunisian population.[26] However, studies from Spain and the Arab communities including that of United Arab Emirates, Jordan, Israel and Tunisia showed an increase prevalence of pregnancy loss in consanguineous marriages as compared to nonconsanguineous ones.[27–32]

Interestingly another study conducted in Pakistan showed lower rates of foetal loss in families where consanguinity is customary across successive generations.[33] It deems necessary to conduct further studies, to clear this ambiguity about the adverse effect of consanguinity on the foetal loss. The possible cause for such diverse findings is not clear. Since aetiology of RFL is multifactorial in which several genetic and environmental factors play their role hence it is possible that several contributing genes, polymorphisms in these genes or their mutations are influencing the occurrence of miscarriages. The prevalence and types of gene mutations and polymorphisms differ in different ethnic groups, similarly the prevalence of RFL also differs. Furthermore, there is increase chance of co-inheritance of abnormal mutations from the two parents in consanguineous marriage, resulting in a homozygous state, thus it may influence the prevalence of RFL. In addition, environmental factors such as lifestyle and food habits also influence the pregnancy outcome. More recently, epigenetic factors have also been found to play the role in the aetiology of several diseases, and such factors may also be contributing to RFL.

CONCLUSION

Despite advocacy for discouraging cousin marriages the consanguineous marriages are in practice for several generations and continue to be so in our population. The cousin marriages seem to offer couples and the families, and even communities some benefits in terms of the security to the spouses both material and emotional, stability of marriage, acceptability by the parents, siblings at home and immediate and extended family and better assurances in terms of family assets, solidarity, and social cohesion.

Although our study does not show any significant harmful effect of consanguinity on foetal outcome, however more in-depth research is required to look for genetic loci which are contributing to the causation of RFL, especially those inherited recessively, since homozygosity is increased in consanguinity. These studies can be conducted in communities traditionally preferring cousin marriages like ours and future genetic studies may be carried out on larger sample to elaborate its effect further and to develop genetic counselling services in health facilities and to disseminate information and educate the people about their health queries.

AUTHORS' CONTRIBUTION

RI: Conceptualization, Study Design, Data analysis, Writeup. AR: Data analysis, Writeup. AF: Data collection, Data entry, Writeup

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