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Consanguineous Marriages

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EFFECT OF CONSANGUINEOUS MARRIAGES ON PERINATAL OUTCOME

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ABSTRACT

Objective: To identify the characteristics of women in consanguineous marriage and their effects on reproductive behavior, adverse pregnancy and fetal outcomes.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: Department of Obstetrics and Gynaecology, Pak Emirates Military Hospital, Rawalpindi, from Jan 2017 to Oct 2017.

Methodology: After fulfilling the inclusion and exclusion criteria, patients were divided into two groups, consanguineous and non-consanguineous group. Data was collected at the time of delivery, whether vaginal delivery or cesarean section. It included demographic profile and clinical factors. Then all the newborn babies were followed up to discharge from the hospital for neonatal outcomes.

Results: There were 1381 participants included in the study. First cousin marriages accounted for 31.1%, second cousin marriages 14.3% and those not in relation were 54.6%. Consanguinity had significant association with age (p=0.03) and ethnicity (p=006). Significant association with consanguinity was found for threatened preterm labour (p=0.04), preterm delivery (p=0.04), nursery admissions (p<0.01), and neonatal outcomes (p<0.01). Low education was found to be 2.46 times more likely to be with consanguinity. Pathan ethnicity gave 1.75 times positive association. Amongst neonatal outcome measures, early neonatal deaths were found two times more likely for consanguinity as compared to non-consanguinous cases.

Conclusion: Consanguinity is very common in Pakistan especially in some ethnic groups. Despite targeting a homogenous group, consanguineous marriages were associated with much higher risk of neonatal intensive care unit admission, stillbirth, perinatal mortality and congenital abnormalities.

Keywords: Consanguinity, Neonatal outcomes, Pregnancy.

INTRODUCTION

'Consanguineous' is defined from the Latin word meaning 'of the same blood'. It is paradoxical that disbelief as to the suitability of first-cousin marriage was upraised by Charles Darwin who was married to his 1st cousin and lost 2 out of his 10 children[1]. Consanguineous marriages peak in most traditional populations. In some nations they are scrupulously avoided, while for the remaining they are positively preferred. Universally the family remains the chief source of social security[2]. For communities that prefer consanguineous marriage, multiple family ties confer strong shared obligation. A review of Islamic text reveals non reinforcement of consanguineous marriage. It is an inherent, respected, deep-seated social trend in some communities. We must distinguish between what is permitted and what is advocated[3]. Consanguinity is among one-fifth of the world population, mostly residing in the Middle East, West and south Asia, Asia and North Africa, as well as among emigrants from these communities now residing in North America, Europe and Australia. In these regions, intra-familial unions collectively account for 20–50% of all marriages. An increased rate of congenital anomalies and autosomal recessive disorders is linked to such practice. These include inborn errors of metabolism, deafness, retinal dystrophies, intellectual and developmental disability, and complex congenital heart disease[4].

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Consanguinity is desired due to significant social and economic advantages which seemingly compensate the disadvantages. Cultural values and cultural continuity is strongly diffused and promoted by consanguinity[5]. Prosperity and social stability diminish the requisite for such strong family ties, and economic advancement might ultimately reduce the occurrence of marriage between cousins. Infact, the slackening of family ties is a familiar social problem of high-resource societies[6]. Western societies percieve consanguinity as causing physical and mental incapacity. These attitudes area heritage of the eugenic trends of the early twentieth century. It is therefore not surprising that cousin marriages are legally banned in 24 out of 50 states of the United States of America but theyare not illegal according to UK law[4].

In Dutch Civil Law, marriages between first cousins are permitted. A sanction on consanguineous marriages is under consideration by the present government to fight forced marriages. Generally, there is a consistent association between consanguineous marriages low socio-economic status, illiteracy and rural residence. These associations increase the burden of confounding factors. There is a substantial literature on the inbreeding effects of consanguinity on human reproduction and health of progeny. The results however are are divergent. Many studies have demonstrated that consanguineous marriages are associated with higher risk of autosomal recessive diseases and congenital malformations, mental retardation, higher pre-reproductive deaths, low birth weight and higher postnatal mortality among off spring. The discrepancy in the results of the above-mentioned studies may be ascribed to organizational flaws, namely small sample size and poor allowance for potential confounders. The association still remains inconclusive. Even after controlling for relevant socio-demographic factors in multivariate analysis, fertility, childhood mortality and fetal loss showed no significant association with consanguinity in Oman[6].

In Pakistan and many other developing countries is, therefore, often proposed that consanguineous marriage should be discouraged on medical grounds. However, several professional groups have pointed out that this proposition is not compatible with the ethical principles of genetic counselling, ignores the communal position of consanguineous marriage and is liable to be unproductive[7]. So the present study has been conducted to examine the pattern and characteristics of women in consanguineous marriage and its effects on reproductive behavior, adverse pregnancy and fetal outcomes.

METHODOLGY

This comparative cross sectional study was carried out in the department of Obstetrics and Gynaecology, Pak Emirates Military Hospital Rawalpindi, over the period of 10 months, between January to October 2017.

Sample size was estimated using online sample size calculator openepi version 3.01 after assuming 50% effect of consanguineous marriages on parinatal outcomes with 2.65% margin of error at 95% confidence interval we required at least 1366 samples for this study as minimum. We used non probability purposive sampling technique due to specific inclusion criteria of samples. Ethical approval was taken from hospital's Ethics committee after negotiations. A total of 1366 pregnant women were included in the study. All the pregnant women with singleton pregnancies coming to labour ward for

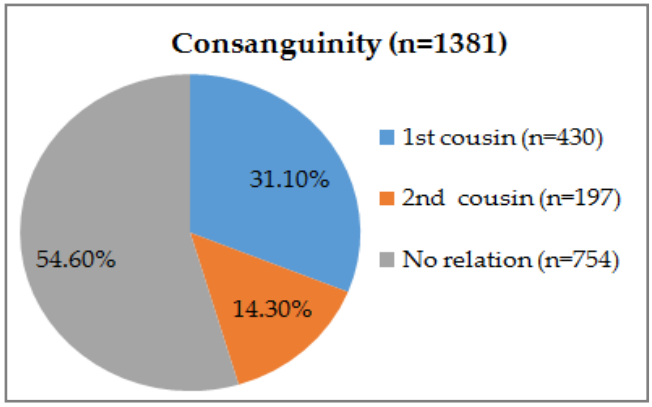

Figure: Distribution of consanguinity among study groups.

delivery or going for caesarean section (excluding private patients) with gestational age greater than or equal to 26 weeks (to exclude miscarriages) were included in the study.

We tried to remove the confounders like low socioeconomic status, illiteracy and rural residence. So it was ensured that; They belonged to same social class and had access to free health services, and They had same level of spousal literacy.

Patients were divided into two groups, consanguineous and non-consanguineous group. Data was collected at the time of delivery from hospital. Perinatal outcomes were measured in terms of Low birth weight (LBW), congenital abnormalities, neonatal intensive care unit (NICU) admissions and neonatal outcomes which included early recovery, intrauterine death (IUD) and early neonatal deaths (ENND).

SPSS-23 was used to analyse the data. Pearson chi square test was used to assess the association of consanguinity with different covariates and perinatal outcomes. Frequency along with percentages were calculated for all qualitative variables.

To measure the adverse effects of in-

Table-I: Association of consanguinity with baseline characteristics of participants.

Characteristics			Consanguinity			*p*-value
			1st cousin (n=430)	2nd cousin (n=197)	No relation (n=754)	
			n (%)	n (%)	n (%)	
Age	16-19 years	n=33	8 (1.9)	3 (1.5)	22 (2.9)	0.03*
	20-24 years	n=326	116 (27)	52 (26.4)	158 (21)	
	25-30 years	n=578	181 (42.1)	67 (34)	330 (43.8)	
	>30 years	n=444	125 (29.1)	75 (38.1)	244 (32.4)	
Age at marriage (Years)	15-19	n=375	115 (26.7)	52 (26.4)	208 (27.6)	0.997
	20-24	n=828	258 (60)	120 (60.9)	450 (59.7)	
	25-30	n=159	50 (11.6)	23 (11.7)	86 (11.4)	
	>30	n=19	7 (1.6)	2 (1.0)	10 (1.3)	
Education	<Primary	n=302	105 (24.4)	51 (25.9)	146 (19.4)	0.12
	Middle	n=510	160 (37.2)	70 (35.5)	280 (37.1)	
	Matric	n=394	122 (28.4)	52 (26.4)	220 (29.2)	
	Intermediate	n=109	29 (6.7)	18 (9.1)	62 (8.2)	
	Graduate	n=66	14 (3.3)	6 (3.0)	46 (6.1)	
Ethnicity	Pathan	n=215	86 (20)	35 (17.8)	94 (12.5)	0.006*
	Hindko	n=83	27 (6.3)	14 (7.1)	42 (5.6)	
	Punjabi	n=814	250 (58.1)	118 (59.9)	446 (59.2)	
	Saraiki	n=64	18 (4.2)	8 (4.1)	38 (5.0)	
	Kashmiri	n=132	28 (6.5)	12 (6.1)	92 (12.2)	
	Other	n=73	21 (4.9)	10 (5.1)	42 (5.6)	

*$p \leq 0.05$ was considered using Pearson Chi Square test

whether vaginal delivery or cesarean section. Demographic data includes patient's age, education, ethnicity andage at marriage. Clinical factors included parity, previous miscarriages, history of any contraceptive use, pregnancy induced hypertension (PIH), threatened preterm labour (PTL) and preterm delivery. All the newborn babies were followed up to discharge

breeding, socio-demographic variables such as maternal age, birth interval needs to be controlled. So logistic regression analysis was done to estimate the odds ratio with 95% confidence interval for all those parameters known to be contributors to poor perinatal outcomes. The *p*-value ≤0.05 were considered statistically significant.

RESULTS

In the present study, there were 1381 participants. First cousin marriages accounted for 31.1%, second cousin marriages contributed 14.3%, and those not in relation with consanguinity were 54.6%, (fig-I). Majority of the participants were between 25-30 years of age (40%) and many participants reported the age at marriage to be 20-24 years (60%). Around 37% were educated upto middle and 58.9% were Punjabi.

Clinical parameters of our study population included history of single miscarriages (18.2%), history of any contraceptive use (8.1%), primigravidity (31%), PIH (11.1%), threatened preterm labour (5.4%) and preterm delivery (8%). Neonatal outcomes included LBW (3.5%), anomalous babies (4.3%), NICU admissions (34%) and ENND (3.9%). Table-I has shown that consanguinity had significant association with age (p=0.03) and ethnicity (p=006).

Clinical parameters which were found to be significantly associated with consanguinity were threatened PTL (p=0.04), preterm delivery (p=0.04), NICU admissions (p<0.01), and neonatal outcomes (p<0.01) table-II.

Table-II: Association of consanguinity with clinical parameters and perinatal outcomes.

Characteristics			Consanguinity			*p*-value
			1st cousin (n=430)	2nd cousin (n=197)	No relation (n=754)	
			n (%)	n (%)	n (%)	
Threatened pre-term labour	Yes	n=74	30 (7.0)	14 (7.1)	30 (4.0)	0.04*
Pregenancy induced hypertension	Yes	n=153	44 (10.2)	21 (10.7)	88 (11.7)	0.73
Low birth weight	Yes	n=49	13 (3.0)	8 (4.1)	28 (3.7)	0.757
Preterm delivery	Yes	n=111	43 (10.0)	20 (10.2)	48 (6.4)	0.04*
Anomalous baby	Yes	n=60	24 (5.6)	12 (6.1)	24 (3.2)	0.065
Chronic Obstructive Pulmonary Disease admission	Yes	n=469	168 (39.1)	83 (42.1)	218 (28.9)	<0.001*
Neonatal outcomes	Recovery	n=1301	407 (94.7)	192 (97.5)	702 (93.1)	<0.001*
	ENND	n=54	8 (1.9)	2 (1.0)	44 (5.8)	
	IUD	n=26	15 (3.5)	3 (1.5)	8 (1.1)	
Parity	0.00	n=428	132 (30.7	66 (33.5)	230 (30.5)	0.89
	1.00	n=399	124 (28.8)	57 (28.9)	218 (28.9)	
	2.00	n=310	92 (21.4)	38 (19.3)	180 (23.9)	
	3.00	n=153	50 (11.6)	19 (9.6)	84 (11.1)	
	4.00	n=55	18 (4.2)	11 (5.6)	26 (3.4)	
	5.00	n=15	6(1.4)	3 (1.5)	6 (0.8)	
	6.00	n=21	8 1.9)	3 1.5)	10 1.3)	
Miscarriages	0.00	n=993	307 (71.4)	134 (68.0)	552 (73.2)	0.92
	1.00	n=252	78 (18.1)	37 (18.8)	137 (18.2)	
	2.00	n=63	22 (5.1)	13 (6.6)	28 (3.7)	
	3.00	n=39	12 (2.8)	7 (3.6)	20 (2.7)	
	4.00	n=23	8 (1.9)	4 (2.0)	11 (1.5)	
	5.00	n=5	2 (0.5)	1 (0.5)	2 (0.3)	
	6.00	n=6	1 (0.2)	1 (0.5)	4 (0.5)	
Contraceptive use	Yes	n=112	29 (6.7)	12 (6.1)	71 (9.4)	0.14

*p≤0.05 was considered using Pearson Chi Square test

After logistic regression analysis, it was found that older age group had 1.65 times positive association with consanguinity. Participants with lesser education were found to be 2.46 times more likely to be with consanguinity. Pathan ethnicity gave 1.75 times positive association with consanguinity as compared to other ethnicities.

Threatened preterm labour, preterm delivery, anomalous babies and NICU admissions were also found to be positively correlated with consanguinity. Amongst neonatal outcome measures, ENND cases were found two times more likely for consanguinity as compared to non-consanguineous cases. Contraceptive use had no correlation with consanguinity table-III.

Table-III: Odds ratio with 95% confidence interval for consanguinity.

Risk Factors		Odds Ratio (95% C.I)	*p*-value
Age (years)	16-19 years	Reference	
	20-24 years	2.13 (4.53,1)	0.06
	25-30 years	1.51 (3.16,0.72)	0.29
	>30 years	1.64 (3.47,0.78)	0.2
Education	<Primary	2.46 (4.36,1.39)	0.01*
	Middle	1.89 (3.29,1.09)	0.03*
	Matric	1.82 (3.19,1.04)	0.04*
	Intermediate	1.75 (3.34,0.92)	0.1
	Graduate	Reference	
Ethnicity	Pathan	1.75 (2.99,1.02)	0.049*
	Hindko	1.33 (2.5,0.71)	0.39
	Punjabi	1.12 (1.82,0.69)	0.66
	Saraiki	0.93 (1.84,0.47)	0.83
	Kashmiri	0.59 (1.07,0.33)	0.09
	Other	Reference	
Threatened pretermlabour	Yes	1.83 (2.94,1.14)	0.02*
Preterm delivery	Yes	1.65 (2.44,1.12)	0.02*
Anomalous baby	Yes	1.86 (3.15,1.1)	0.03*
Neonatal intensive care unit admission	Yes	1.65 (2.06,1.32)	0.01*
Neonatal outcomes	Recovery	Reference	
	Early neonatal death	0.27 (0.54,0.14)	0.01*
	Intra uterine death	2.64 (6.11,1.14)	0.03*
Contraceptive use	Yes	0.68 (1.01,0.46)	0.06

*$p \leq 0.05$ was considered significant using binary logistic regression, Dependent variable: consanguinity

DISCUSSION

Consanguineous unifications are more prone to have cognitive decay in KSA and Southern India. Studies steered in the British Pakistani population corroborate these results[5]. Using a representative sample of 3,203 (grade 4 and grade 6) children from the Arab educational system in Israel[8], finds that when it comes to cognitive testing, the offspring of double-cousin marriages perform the worst. We did not analyze the double consanguineous data separately. However, in some ethnic groups there were multiple loops of consanguinity in previous generations, also an elevated risk of malformations. In southern India and among groups with a socio-economic disadvantage, a chief predictor of adverse pregnancy outcomes is consanguineous marriages, which is in line with the results of our study.

A meta-analysis of 38 studies, mostly from countries considered to have low resources, revealed an average 4.4% increase in infant mortality among the children of first cousins,

compared with unrelated controls[4]. It should, however, be apprehended that death due to congenital disorders may be due to inadequate treatment in countries with low resources; on the other hand, countries with more resources would be more likely to treat such disorders. Several studies have highlighted that that fertility rate is slightly higher but miscarriage rate is not different in consanguineous marriages. We observed no difference in miscarriage rates and further on, no statistically significant difference in age at marriage in consanguineous group. Baseline 2.0-2.5% birth prevalence of serious congenital and genetic disorders, for children of unrelated parents, is increased to 4-6.5%. Stillbirths and infant mortality rates are alsogreater. Birth defects frequency is estimated to be around 3-3.5% higher[4,9]. Our study also mirrored the same trend.

According to famous Birmingham study, among the North European children the birth prevalence of all congenital and genetic disorders was 4.3%, and that of definite, probable and possible recessive disorders was 0.28% (6.5% of the total). Among British Pakistani children, the birth prevalence of all congenital and genetic disorders was 7.9% almost twice as high as among North Europeans-whereas the prevalence of definite, probable or possible recessive disorders was 3.0–3.3% over ten times higher than among North Europeans[10]. The study liberally confirms that populations in which such marriages are more likely carry a higher genetic risk and have increased needs for services specific to genetic counselling[11]. The same recommendation would hold true for our study.

Successful role model are Iran and Saudi Arabia focused on detection of carriers and promotion of counseling, in order to prevent certain disabilities[12,13]. In Bahrain, a curtailment in prevalence of sickle cell anaemia was found to be 70% over 20 years and first-cousin marriage prevalence reduced from 24 to 9%. But negative effects of consanguinity on children's cognitive ability may not be necessarily addressed by these interventions[10,14].

Employing anexceptional household survey from Pakistan, there wasrobust evidence linking consanguinity to lower cognitive abilities and higher incidence of severe stunting among children. According to a paper from world bank, there is an approximately 4.4% increased risk for pre-reproductive mortality above the population background risk, some of which include major congenital defects. The risk for an adverse health outcome is greatest in the 1st year of life[7]. Our study did not follow the offspring to confirm such an association. However in variance to other studies we did not find an association with low educational status, early marriage and low contraceptive uptake. The reason is that we targeted only wives of lower ranks in military. It was a homogenous group with same socioeconomic class and similar access to free health services.

The closer the relationship between parents, the more likely it is that their off spring will inherit identical copies of one or more detrimental recessive genes. For example, first cousins are predicted to share 12.5% (1/8) of their genes. Thus, on average, their progeny will be homozygous at 6.25% (1/16) of gene loci[12,15]. The results of our study are also in agreement. Closer consanguineous relationship such as a double first cousins couple may be given a higher risk for their offspring which may be estimated to triple the rate of birth defects in the general population. This has been shown in our study as well. Hence, consanguinity both poses reproductive risks and also raises the burden of child and healthcare and family expenses; therefore we can infer detrimental effects on the finances and productivity of the entire family[16].

Consanguineous couples are more prone to have children with metabolic disorders and medical disorders[17-20]. In India, all types of adverse pregnancy outcomesdisplayeda greater prevalence among consanguineous mothers compared to non-consanguineous mothers. A research in Pakistan found that first cousin marriages were more prone to experience a child's death[21]. These results are in line with the

findings of our study. Consanguineous couples may keep their relationship hidden because of fears of stigma, discrimination and even legal prosecution. Discoursing such fears and the approaches of family and friends regarding their relationship is important.

Targeted education programs enhance community awareness and have led to decline in consanguineous marriages. A decline in close biological kin marriage is reported in Saudi Arabia, Turkey and Jordan but that is not the case in Iran.

CONCLUSION

Consanguinity is very common in Pakistan especially in some ethnic groups. Despite targeting a homogenous group, consanguineous marriages were associated with much higher risk of NICU admission, stillbirth, perinatal mortality and congenital abnormalities.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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