ORIGINAL RESEARCH ARTICLE

Consanguinity as a predictor of premature births reported in maternity wards of teaching hospitals in Sindh Pakistan

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Abstract

This hospital based comparative study was conducted in a populous cities of Sindh, Pakistan. The study aimed to assess prevalence of consanguinity and to determine association of consanguinity with premature births. The 962 recently delivering mothers were selected through convenience sampling. The socio-demographic predictors of premature births were sorted by bivariate analysis. The logistic regression modelling was done to compare odds ratios at 95% confidence intervals for the association between consanguinity and premature birth. The prevalence of consanguinity was 57.38%; the 47.82% of pregnancies in first cousin couples resulted in premature births (odds ratio 4.34). Younger maternal age i.e. < 25 years, addiction to betel nuts and inadequate antenatal care (Odds ratios 1.90, 2.89 & 1.84 respectively) were identified as potential statistically significant confounders. The adjusted odds ratios of premature births among first and second cousin couples were 4.22 & 1.62 i.e. P < 0.01 and P < 0.05, respectively. The study highlights an increase in preterm births in consanguineous couples. (*Afr J Reprod Health 2023; 27 [9]: 127-133*).

Keywords: Consanguinity, premature birth, predictor, birth outcome, adverse birth outcome

Résumé

Cette étude comparative en milieu hospitalier a été menée dans des villes peuplées du Sind, au Pakistan. L'étude visait à évaluer la prévalence de la consanguinité et à déterminer l'association de la consanguinité avec les naissances prématurées. Les 962 mères ayant récemment accouché ont été sélectionnées par échantillonnage de convenance. Les prédicteurs sociodémographiques des naissances prématurées ont été triés par analyse bivariée. La modélisation de régression logistique a été réalisée pour comparer les rapports de cotes à des intervalles de confiance de 95 % pour l'association entre la consanguinité et la naissance prématurée. La prévalence de la consanguinité était de 57,38 % ; les 47,82% des grossesses chez les couples cousins germains ont abouti à des naissances prématurées (rapport de cotes 4,34). Un âge maternel plus jeune, c'est-à-dire < 25 ans, une dépendance aux noix de bétel et des soins prénatals inadéquats (rapports de cotes 1,90, 2,89 et 1,84 respectivement) ont été identifiés comme facteurs de confusion potentiels statistiquement significatifs. Les rapports de cotes ajustés des naissances prématurées parmi les couples de cousins germains étaient de 4,22 et 1,62, soit P < 0,01 et P < 0,05, respectivement. L'étude met en évidence une augmentation des naissances prématurées dans les couples consanguins. (*Afr J Reprod Health 2023; 27 [9]: 127-133*).

Mots-clés: Consanguinité, naissance prématurée, prédicteur, issue de la naissance, issue défavorable de la naissance

Introduction

Consanguinity has remained humans' preferred reproductive strategy and a matter of human biological inquiry since many centuries. Linguistically, this term describes children born to couples having a close common ancestor¹. As of 2010, the 10.4% of the global population was practicing consanguinity² and 101 million more

people are to continue the same practice as they were residing in countries where consanguinity was highly prevalent³. Many nations permit marriage between first cousins as preferred cultural practice⁴. It was conservatively estimated that first cousin marriages were most prevalent form of intrafamilial unions⁵. However, despite a decline in consanguinity in societies with strong intra-familial traditions evidenced during late 19th and early 20th centuries, the premature births are still reported as important adverse birth outcome⁶.

The World Health Organization (WHO) defines prematurity as birth occuring before 37 weeks of gestation⁷. Despite major preventive measures, premature births are on the rise globally. the reported proportional premature live births were 12% and 9% in developing and developed countries, respectively⁸. Pakistan with annual average of 15.8% premature births, ranks at eighth number worldwide⁹. Consanguinity is considered as a risk factors for slow decline in premature births^{10,11}. The consanguineous couples are reported to carry 1.6-fold increased risk of giving birth to premature babies at least once in their reproductive lives thereby adding to the pool of premature births¹. This is due to variety of genetic disorders arising from exchange of genes from the common ancestors¹². The study was aimed at determining the prevalence of consanguinity and its effect on preterm birth.

Methods

Participants and data sources

This hospital based prospective study was carried out in randomly selected public & private maternity hospitals in Hyderabad & Jamshoro cities of Sindh Pakistan. The study was conducted from June 2016 to March 2017.

The average prevalence of consanguinity in Pakistan was reported as 40 percent¹³ therefore 370 sample size was computed for consanguineous & non-consanguineous groups each by applying formula of single population proportion. In order to accomodate the non-response rate, controlling the confounders, missing data and misreporting etc. at 95% confidence level and 5% margin of error, 30% more participants were recruited resulting in total required sample size as 962. The subjects i.e. recently delivered women in prior designated hospitals were selected through non-probability convenience sampling. Information on consanguinity was self-reported by the subjects. Consanguineous marriages were defined as marriages between those descended from the same ancestor. For the purpose of the study, consanguinity was defined as a union between a couple related as second cousin or closer, equivalent to a coefficient of inbreeding (F) \geq

0.0156: (Consanguinity categories were identified from the information collected: uncle-niece (F =0.125), first cousin (F = 0.0625), second cousin (F = 0.0156)). Lineal as well as collateral consanguinity was recorded with the help of pedigree. Only the first cousin, second cousin and uncle-niece relations of spouses were recorded as consanguineous status. The couples having blood relation beyond second cousin or having common ancestor three or more generations above, were labelled as non-consanguineous. The consenting women of any parity, age 18-45 years, who have recently given birth to singleton baby at any gestational age were recruited in study to observe the relationship between various degrees of consanguinity and premature births.

Data collection

Data were collected on structured, validated questionnaire having close ended questions. The English version of questionnaire was translated in local languages (Urdu & Sindhi). This was retranslated in English to check its consistency. Pilotting was done on 90 subjects, the results of pilot study were not included in this study. The parents / guardians of the new born delivered at maternity wards of the designated hospitals were the primary source of information. Data sources included direct interviews conducted by the authors themselves. The participants' hospital records were also the part of the data. Before collecting data. written permission was obtained from Research Ethics Committee of Liaguat University of Medical and Health Sciences. The permission was also obtained from administrators of all designated hospitals. The written informed consent was received from all subjects along with their signatures/thumb impressions after assuring them about maintenance of confidentiality of information shared by them. The data completeness & consistency was checked on daily basis.

Statistical analysis and data interpretation

After editing and cleaning of data in microsoft excel and checking for its integrity, the results were compiled in SPSS version 22.0 (IBM Corp.,Armonk, NY, USA). Frequencies and percentages were computed to describe qualitative variables. The univariate analysis of data was done

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in terms of consanguineous degrees and premature births. The bivariate analysis of selected degrees of consanguinity was done to estimate an association with premature births. Considering the intrauterine deaths as confounding factor for the associations, separate analysis of the association between consanguinity and premature births were performed after including & excluding the intrauterine deaths within two subgroups.

The potential covariates for premature births were identified on the basis of cut-off *P*-values ≤ 0.10 . Finally, in the light of above analysis, logistic regression models were constructed by incorporating the potential predictors affecting the associations among two comparison groups. The odds ratios of premature birth as a measure of association at 95% confidence intervals and P-value < 0.05 on the two-tailed analysis was considered to indicate statistical significance.

Results

Distribution of consanguinity and premature births

Table 1 shows the information related to distribution of degrees of consanguinity and premature births. Among consanguineous group of subjects, there was slight preponderance of first cousin couples (47.82%) as compared to second cousin and uncle-niece couples i.e. 41.67% and 10.51%, respectively. Premature live births were observed five times more frequently to consanguineous couples. The highest number of premature live births was recorded among the new born of parents related as uncle-niece (20.40%).

Table 2 shows unadjusted risk estimation of being born as live premature among new borns delivered to various groups of consanguineous couples after excluding 83 cases of intrauterine deaths. Unadjusted odds ratio of 4.34 (95% CI 2.33, 8.06; P < 0.01) was shown among offsprings of parents related as first cousin. Table 3 shows that after including eighty three cases of intrauterine deaths, the unadjusted odds ratio were computed as 4.19 (95% CI 2.58,6.80; P < 0.01) and 1.59 (95% CI 1.07, 2.38; P < 0.001) among offsprings of first cousin and second cousin couples, respectively.

Table 3 shows unadjusted risk estimation of being prematurily born delivered to various

 Table 1: Consanguineous status and premature live

 births

Consanguineous status	Frequencies	Premature	
	(%)	live births	
Consanguineous	552 (57.38%)	74 (15.38%)	
First cousin	264 (47.82%)	36 (16.28%)	
Second cousin	230	28 (13.27%)	
Uncle-niece	(41.67%)	10 (20.40%)	
	58 (10.51%)		
Non-consanguineous	410 (42.62%)	15 (3.76%)	
Total	962 (100%)	89 (9.25%)	

groups of consanguineous couples including 83 cases of intrauterine deaths.

Table 4 depicts bi-variate analysis of expected covariates for premature births showing maternal age <25 years (OR 1.90; 95% CI 1.08, 2.32; P=0.04), rural/slum residence (OR 1.35; 95% CI 1.86,2.12; P=0.04), addiction to take betel nuts (OR 2.89; 95% CI 1.73,3.84; P=0.04) and inadequate antenatal care (OR 1.84; 95% CI 0.90,3.76; P=0.09) identified as potential confounders. Table 5 depicts final results after incorporating the potential confounders.

Discussion

In Pakistan consanguinity is a deeply rooted sociocultural trend therefore this country provides an interesting ground and opportunity of research exploring association of consanguinity with adverse birth birth outcomes. This country falls into the third category based on the prevalence of consanguinity varying between 10-50 percent¹⁴. despite declining tendency Here, of consanguineous marriages, its prevalence is still alarmingly high i.e. 31.12 to 60 percent¹⁵; which is due to an elevated rate of consanguinity in some pockets of communities. Another study revealed it at even higher rates ¹⁶. It was therefore important to study the effects on the newborn delivered to couples in first cousin, second cousin and uncleniece spousal relation. The current study revealed rates as 47.82%, 41.67% and 10.51% among first cousins, second cousins and uncle-niece spousal relation, respectively.

The uncle-niece union is reported by some researchers as practiced at rate around 14 percent ¹⁷. Past studies reveal this figure as high as 20+ percent¹⁸. In one study, the 61.3% subjects were

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Consanguineous	Total	Premature	Odds ratio	95% CI	<i>P</i> -value
Consanguinity	481	74	0.21 ^a	0.12 - 0.38	0.001**
First cousin	221	36	4.34 ^b	2.33 - 8.06	0.004**
Second cousin	211	28	0.25 ^a	0.13 - 0.49	0.001**
Uncle-niece	49	10	0.15 ^a	0.06 - 0.36	0.003**

Table 2: Association of consanguinity to premature births (excluding intrauterine deaths)

^a Unadjusted odds ratio < 1.0

^b Unadjusted odds ratio > 1.0 ** Significant findings at *P*: < 0.01

 Table 3: Association of consanguinity to prematurity (including intrauterine deaths)

Consanguineous	Total	Premature	Odds ratio	95% CI	<i>P</i> -value
status		births			
Consanguinity	552	167	0.19 a	0.12 - 0.30	0.002 **
First cousin	264	77	4.19 ^b	2.58 - 6.80	0.004 **
Second cousin	230	47	1.59 ^b	0.13 - 0.49	0.003 **
Uncle-niece	58	17	0.16 ^a	0.08 - 0.32	0.004 **

a Unadjusted odds ratio < 1.0
 b Unadjusted odds ratio > 1.0

** Significant findings at *P*: < 0.01

Table 4: Relation of prematurity and expected predictors

Expected predictors	Attributes	Premature	Odds ratios ^a	95% CI	P-values
		births			
Maternal age	Yes 187 (21.28%)	24	1.90	1.08 - 2.32	0.04*
< 25 years	No 692 (78.72%)	65			
Maternal illiteracy	Yes 561 (63.82%)	57	0.99	0.62 - 1.56	0.97
	No 318 (36.18%)	32			
Low socio-	Yes 449 (51.09%)	51	0.68	0.44 - 1.07	0.09
economic status	No 430 (48.91%)	38			
Rural / slum residence	Yes 588 (66.89%)	54	1.35	1.86 - 2.12	0.04*
	No 291 (33.11%)	35			
Poor maternal	Yes 623 (70.87%)	59	1.26	0.79 - 2.01	0.32
nutritional status	No 256 (29.13%)	30			
Maternal anemia	Yes 746 (84.86%)	81	0.52	0.24 - 1.11	0.09
	No 133 (15.14%)	8			
Smoking habits in	Yes 29 (3.30%)	2	1.53	0.35 - 6.57	0.56
mother	No 850 (96.70%)	87			
Addiction of betel nuts	Yes 361 (41.07%)	38	2.89	1.73 - 3.84	0.04*
	No 518 (58.93%)	51			
Maternal chronic	Yes 205 (23.32%)	28	0.62	0.39 - 1.01	0.05
diseases	No 674 (76.68%)	61			
Birth interval < 2 years	Yes 415 (47.21%)	36	2.50	0.59 - 10.50	0.21
for current pregnancy	No 464 (52.79%)	53			
Inadequate ante-natal	Yes 734 (83.51%)	9	1.84	0.90 - 3.76	0.09 †
care (0-1)	No 145 (16.49%)	80			
High birth order \geq 3	Yes 533 (60.64%)	35	2.50	0.59 - 10.50	0.21
	No 346 (39.36%)	54			
Gender (being female)	Yes502 (57.11%)	46	1.27	0.82 - 1.98	0.27
	No 377 (42.89%)	43			
External birth defects	Yes 58 (6.59%)	4	1.55	0.55 - 4.41	0.40
	No 821 (93.41%)	85			

^a Unadjusted odds ratios

* *P*: < 0.05 ; † *P*: < 0.1

Table 5: Association between premature birth for current pregnancy in consanguineous new born after incorporating potential predictors

	Total	Premature births	Odds ratio ^a	95% CI	P-values
Consanguinity	552	167	0.19 ^b	0.12 - 0.30	0.001**
First cousin	264	77	4.22 °	2.60 - 6.86	0.001**
Second cousin	230	47	1.62 °	0.09 - 2.43	0.01*
Uncle-niece	58	17	0.16 ^b	0.08 - 0.32	0.44

^a adjusted Odds ratios (aORs) for maternal age < 25 years, rural residence, addiction to betel nuts and inadequate ante natal care

^b adjusted odds ratio < 1.0

^c adjusted odds ratio > 1.0

* P: <0.05 ** P: <0.01

F. **N**0.01

consanguineously related. The first cousin unions were the highest in proportion and accounted for 50.2% while second cousin marriages were 3.2 percent¹⁹. In addition to the risk of acquiring a recessive genetic disease, the offspring of consanguineous parents are shown to be at an increased risk of premature birth²⁰. The premature live births' prevalence in current study was as 9.25% computed (15.38%) among consanguineous group as compared to 3.76% in non-consanguineous group i.e. 5:1 ratio of occurrence of prematurity among consanguineous non-consanguineously and related parents (Table 1). This finding is quite similar to another study showing 13% premature births recorded in consanguineous group of couples ²¹. This finding is supported by another research conducted in Saudi Arabia and other Middle East countries showing 1.6 fold net increased risk for new born delivered at < 33 weeks of gestation in consanguineously related couples ^{22,23}. The body of literature therefore necessitates the public awareness regarding such a risk factor in planning public health education programs and in considering appropriate care options for women at potentially higher risk of premature delivery. Bivariate analysis of consanguineous status and premature births revealed highly significant association in all groups of consanguinity (P < 0.01). After excluding 83 current pregnancies terminating as intrauterine deaths, the first cousins were found at odds of giving birth to premature babies (OR 4.34; 95% CI 2.33, 8.06; P < 0.01) (Table 2). After incorporating intrauterine deaths in analysis, the odds of giving birth to premature babies in the index pregnancy for second cousin couples were also found statistically significant (unadjusted OR 1.59; 95% CI 1.07, 2.38; *P* < 0.01 and OR 1.94; 95% CI 1.31, 2.86; *P* < 0.001 respectively) (Table 3). Other researches however

presented conflicting evidence regarding effects of consanguinity on premature births²⁴. Some other studies support our findings of consanguinity as a risk for adverse pregnancy outcomes including premature birth⁵. The multiple risk factors contribute towards premature births. A comprehensive analysis was undertaken to separately analyze such predictors (Table 4). Maternal age < 25 years was found as a potential co-variate. Leaving aside the established facts in various studies that consanguinity is associated with younger age at marriage and high fertility, a found uniform and almost equal distribution of maternal age among two groups of study subjects i.e. mean maternal age in consanguineously married women was 28.06 ± 3.02 years and 28.59 ± 3.23 years among non-consanguineous women. The association of younger maternal age (< 25 years) with higher odds of premature births is secondarily due to lesser education level, higher risk behaviors like lack of follow up ante-natal visits and compromised nutritional status²⁵.

potential Among co-variates for association between consanguinity and premature births, living in rural areas was reported to increase the risk of premature births. The present study had almost uniform distribution of subjects living in rural/ slum areas among two groups i.e. 67.57% and 66.34% in consanguineous and nonconsanguineous women respectively. Another epidemiological study conducted on this issue depicted rural mothers having this risk as 1.60 times (95% CI 1.22,2.34; P<0.001) as compared to the mothers residing in urban areas²⁶. The association of place of residence with fetal wellbeing was extensively studied throughout the world and it showed positive correlation with gestational age of new born^{27,28}. The maternal urban residential status is linked to maternal higher level of education,

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availability of good quality ante-natal care services. The maternal education was reported as linearly correlated with pre-term births $(P=0.01)^{25}$. The established findings in worldwide literature documenting the association between maternal educational level and premature births was endorsed by another research which showed that primary educated mothers were more likely to deliver premature babies (OR 1.49; 95% CI 1.02,2.17) as compared to higher education educated mothers²⁶.

Higher maternal education might be related with higher family income and better maternal nutritional status which improve fetal maturity and birth weight. This protective interaction of higher maternal education on maturity of the baby at birth reminds the public health managers to strengthen the adequate ante-natal services at least for the disadvantaged groups. In the current study, regarding educational status among two groups, the proportion of illiterate mothers among consanguineous groups were 68.11% as compared to 59.75% in non-consanguineous group. A better place of residence along with higher level of education and awareness among expectant mothers ensured better outcome in terms of new born health. In this regard, the importance of scheduled antenatal care visits cannot be omitted. There is plenty of literature showing association between getting timely ante-natal care services and delivering new borns at term²⁹.

The chronic consumption of betel nuts by women at child bearing age was lead to prematurity and low birth weight³⁰⁻³². However any national or international literature of such kind was not found to compare the results. It should be noted that there is still dearth of research regarding incorporating all possible confounder to seek association between various degrees of consanguinity and prematurity after simultaneously incorporating such confounders.

Conclusion

The study highlights the high prevalence of consanguinity in Pakistani population. The premature births reported in consanguineous group of couples is quite alarming. The findings from analysis add to the growing scientific literature regarding effect of parental consanguinity on premature births. The consanguineous couples should be priorly informed about the expected risks to their offspring with special reference to birth of a premature baby.

Strengths

The adequate sample size, good response rate, first hand data collected by authors themselves and incorporation of large number of demographic variables were the strengths of this study. Inclusion of different types of parental consanguinity to provide stratified analysis was also strength of this study. The study comprehensively attempts to fill the gap in existing literature by illustrating the prevalence of consanguinity in Pakistani population and elucidating its effect on premature births

Limitations

In authors' opinion, the high representation of subjects from rural/slum areas and the self reporting nature of some variables were the potential limitations of this study.

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Conflict of interest

There are no conflicts of interest.

Data availability

The authors ensure availability of data subject to requirement.

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