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Full Length Research Article

EFFECT OF CONSANGUINITY ON FETAL GROWTH RATIO

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ABSTRACT

Introduction: Marriages between blood relatives are nowadays cultural norms & are least researched in relation to adverse child health outcomes. The fetal growth ratio can be used to demonstrate this effect.
Objective: To determine the effect of consanguinity on fetal growth ratio.
Methods: Cross-sectional data was collected through filling of pre designed questionnaire on three hundred & fifty six consecutive live born singleton newborns delivered in various hospitals in Hyderabad in September 2015. Birth weight was modeled by use of fetal growth ratio & its association with parental inbreeding was analyzed by logistic regression analysis.
Results: Consanguinity was found among 55.4% subjects. The mean growth ratio in consanguineous group was 0.861 ± 0.085 versus 0.941 ± 0.06 among non-consanguineous. The corresponding values for parents inbred & non-inbred were found as 0.859 ± 0.074 & 0.861 ± 0.104 respectively. The logistic regression analysis to predict net effect of inbreeding on fetal growth ratio after controlling for medical and socio-demographic covariates, revealed a statistically significant negative association between parental inbreeding and fetal growth ratio (OR 1.48; 95% C.I 1.033 - 1.591; p=0.04).
Conclusions: Parental inbreeding affects the birth weight of new borne at corresponding age of gestation.

INTRODUCTION

Consanguinity, referred to as the unions between biologically related individuals is a deeply rooted social trend among one-fifth of the world population (Hamamy 2012). Consanguineous marriages are reported to be universal phenomenon as more than one billion people throughout the world are residing in consanguineous accustomed countries (Hamamy, Antonarakis *et al.,* 2011). One in every three marriages throughout the world is between cousins (Rivoisy, Gérard *et al.,* 2012). In the situation when second or higher order related couples and their offspring represent more than 10% of the current world population in general (Taleb, Salem *et al.,* 2015) & in sub-continent Indo-Pak in particular (Mobarak, Kuhn *et al.,* 2013), there is a dire need of research on this aspect of immense public health importance. It has been observed that as Islam allows for consanguineous marriages therefore there is higher prevalence of this phenomenon seen in Islamic countries (Mobarak, Kuhn *et al.,* 2013). It is estimated that consanguineous marriages are widely prevalent in Pakistan i.e. 56.75% (Hina and Malik 2015). In addition to the risk of acquiring a recessive genetic disease, the health of offspring of consanguineous parents is plausibly at an increased risk that necessitates to be investigated. One of the few health risks to newborn is reduction in birth anthropometric measurements including birth weight (Abbas and Yunis 2014). As of our set up, the birth weight does not portray the dynamics of intra utero growth of fetus therefore fetal growth ratio is taken as the most reliable predictor of fetal weight gain with reference to gestational age. The primary health care providers are faced with consanguineous couples demanding answers to their questions on the anticipated health risks to their offspring & the fetal growth ratio (relative fetal weight for gestational age) can be used to demonstrate this effect. The dearth of community based research on this aspect particularly in our country necessitates that research be conducted with the purpose to determine the effect of consanguinity of

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various degrees on fetal growth delivered at various gestational ages.

Hypothesis: Parental consanguinity affects the fetal growth ratio.

Objective

- To determine the prevalence of consanguinity in the study population.
- To determine the effect of consanguinity on fetal growth ratio.

MATERIALS AND METHODS

The study was conducted after approval of the Research Ethics committee of Liaquat University of Medical & Health Sciences, Jamshoro. Before data collection, the departmental permission from administration of hospitals was also obtained. It was a comparative cross sectional study conducted in maternity wards of public & private sector hospitals in Hyderabad including Liaquat University Hospital Hyderabad & Jamshoro, CDF Hospital (Countess of Dufferin Hospital) Hyderabad, Wali Bhai Rajputana Hospital, jijal Maau Hospital Hyderabad. Three hundred & fifty six subjects were approached. Excluding twenty four intrauterine dead babies, cross-sectional data was collected through non-probability consecutive sampling technique on three hundred & thirty two consecutive live born singleton newborns delivered at public & private sector hospitals in Hyderabad. The data was collected by filling a questionnaire comprising of close ended questions arranged in different sections. Prior consent of the parents was taken after ensuring their anonymity & confidentiality of the record. The new borne of age less than 48 hours fulfilling the eligibility criteria were the study subjects; while their parents/ guardian were source of information. The subjects included were live new borne of age ≤ 48 hours, both genders, borne as singletons irrespective of birth weight, gestational age at birth & mode of delivery. Those who were born to consanguineous parents upto 2nd degree & whose parents were in uncle-niece relation were labeled as consanguineous new borne; while others were labeled as non-consanguineous. The subjects who were excluded from study were those who were not willing to participate in study. Twins, still borne, intrauterine dead borne & those borne with apparent congenital abnormality were excluded from the research. The new borne parental inbreeding history was also recorded. The maternal obstetric history records & nursery charts were also used as support documents. The priori confounders expected to affect the results were maternal age, her educational status, parity, birth interval, pre-natal care & family's socio-economic status. Maternal past obstetrical problems, her nutritional status & other behaviors that might affect the outcome variable, were also recorded as co-variates.

Independent variable: Consanguinity upto second degree & uncle-niece relation.
Dependent variable: Fetal growth ratio.

Data was analyzed in SPSS version 16.0. The frequency of consanguinity was calculated as per hundred live births in all maternity wards. Birth weight was modeled by use of the fetal growth ratio i.e. the ratio of the observed birth weight to the median birth weight for gestational age. Means & standard deviations for fetal growth ratios were computed for both groups of new borne. Co-efficient of correlation between fetal growth ratios & gestational weeks were computed for two groups of new borne. The p-values of 0.05 were the cut-off point for level of significance. The fetal growth ratios were converted into categorical variables by categorizing the ratios as <1 & ≥ 1 & their association with various degrees of consanguinity were analyzed by application of logistic regression after incorporating the possible co-variates.

RESULTS

Three hundred & thirty two subjects fulfilling the eligibility criteria were registered for the study. Excluding 24 (6.7%) births ending as intrauterine deaths, consanguinity was found among 55.4% subjects. New borne delivered to first & second cousin parents & uncle-niece relation were labeled as consanguineous. The consanguineous status of the study subjects is depicted in Table 1.

Table 1. Consanguineous status of study subjects

Consanguineous status	Frequency (%)
Consanguineous subjects (total)	184 (55.4%)
1st cousin	80 (24.1%)
2nd cousin	83 (25.0%)
Uncle-niece relation	21 (6.3%)
Non-consanguineous subjects (total)	148 (44.6%)

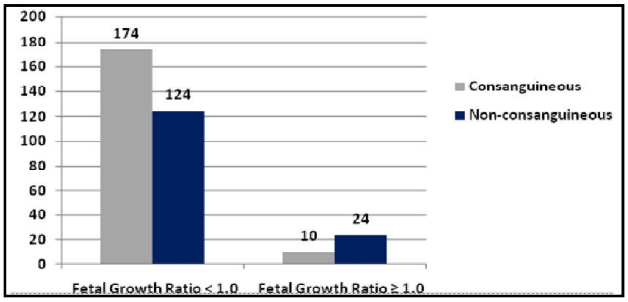

Chart I. Relation Between consanguineous status and fetal growth ratio

The reference median fetal weights at different gestational ages are shown in Table 2a & their corresponding Odds ratios in various levels of consanguinity is shown in Table 2b. The mean growth ratio of consanguineous versus non-consanguineous new borne was 0.861 ± 0.085 & 0.941 ± 0.06 respectively (Chart I, II & II).The corresponding values for parents inbred, mother inbred, father inbred & both parents non-inbred were found as 0.859 ± 0.074, 0.924 ± 0.092, 0.882 ± 0.090 & 0.861 ± 0.104 respectively (Chart IV & V). A mixed-effect logistic regression model with 90.1% accuracy was used to predict the net effect of various types of consanguinity & parental inbreeding on fetal growth ratio. After controlling for medical and socio-demographic covariates such as parity, maternal weight, socio-economic status, birth intervals etc, a statistically significant positive association was observed between parental inbreeding and fetal growth ratio. Overall, consanguinity was associated with a decrease in fetal growth ratio by 14.8% (OR 1.48; 95% C.I 1.033 - 1.591; p=0.04).

Table 2a. Gestational ages and corresponding median fetal weights in Asian population

Weeks of Gestation	Median fetal weight in Grams	Weeks of Gestation	Median fetal weight in Grams
28	1468	35	2383
29	1535	36	2622
30	1584	37	2859
31	1645	38	3083
32	1702	39	3288
33	1918	40	3462
34	2146	41	3486

Global reference for fetal-weight and birthweight percentiles.

Table 2b. Association of various degrees of inbreeding with fetal growth ratio

Variables of Interest	Response	Fetal Growth Ratio < 1 (%)	Odds ratio	95% Confidence interval Lower-upper	p-value
Consanguinity	Yes	174 (94.6%)		0.033 - 1.591	0.136
	No	124 (83.8%)	0.228		
Type of Consanguinity	1st cousin	76 (41.3%)	0.992	0.362- 2.715	0.987
	2nd cousin	79 (42.9%)			
	Uncle-niece	19 (10.3%)			
Father Inbred	Yes	151(45.5%)	1.069	0.374 - 3.057	0.901
	No	147 (44.2%)			
Mother Inbred	Yes	146 (43.9%)	0.269	0.081- 0.895	0.032
	No	152 (47.8%)			
Both parents inbred	Yes	73 (21.98%)	2.422	0.408 - 14.379	0.330
	No	225 (67.7%)			

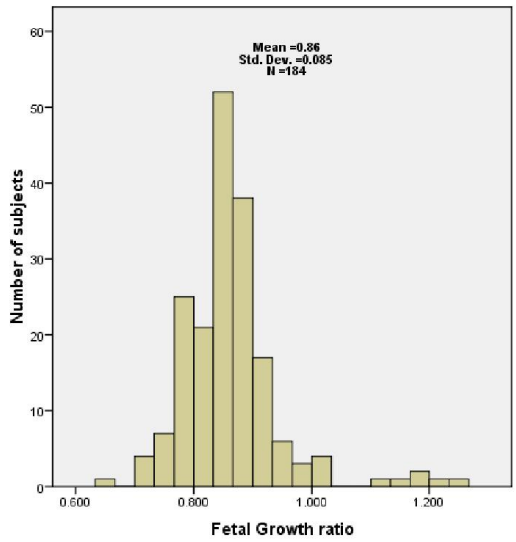

Chart II. Fetal growth ratios of consanguineous new-bornes

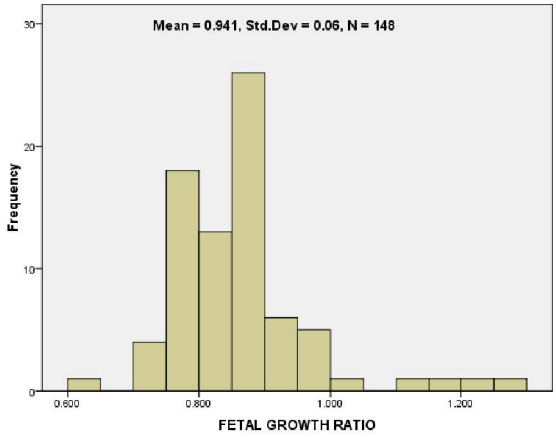

Chart III. Fetal growth ratios of non- consanguineous new-bornes

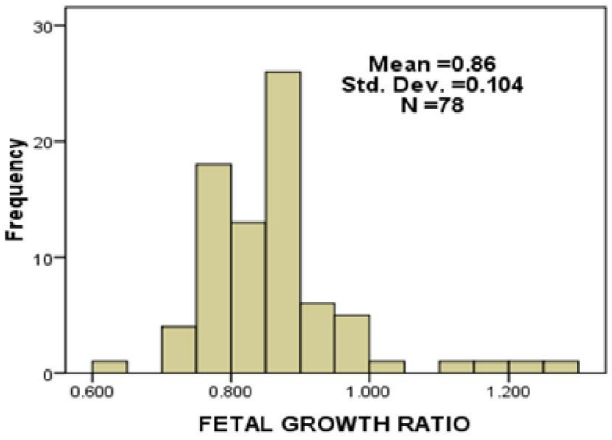

Chart IV. Fetal growth ratios of new bornes of non-inbred parents

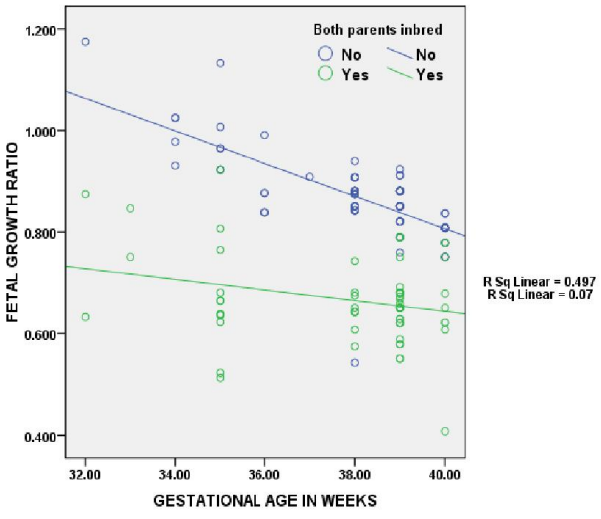

Chart V. Effect of degree of parental consanguinity on fetal growth ratio

DISCUSSION

The 55.4% prevalence of consanguinity is quite comparable to results of similar studies in various Arab countries which show this prevalence as ranging between 44-61% (Na'amnih, Romano-Zelekha *et al.,* 2015) . This is quite in contrast to latest data from developed countries where this prevalence is reported to be as less as 1-2% (Sharkia, Mahajnah *et al.,* 2016). The current study does not reflect the actual prevalence of consanguinity because it was a hospital based study; however it gives an estimation of the prevalence. The more broader community based study will show the real picture of prevalence of consanguinity in our community. Religious relaxation to muslims is one of the major contributing factor behind high prevalence of consanguinity among them although this trend of marriages is now reported to decline (Na'amnih, Romano-Zelekha *et al.,* 2015).The almost equal share of first and second cousin marriages (24.1% & 25.0% respectively) (Table I) is also revealed in other studies conducted throughout the world such as in Iran (Maghsoudlou, Cnattingius *et al.,* 2015), China (Zhang, Li *et al.,* 2012) , Italy (Cavalli-Sforza, Moroni *et al.,* 2004) & Egypt (Yamamah, Abdel-Raouf *et al.,* 2013). In contrast to birth weight, the fetal growth ratio is the most recommended parameter to assess the intrauterine growth pattern of fetus as it takes into account the gestational age of the new borne (Mayer and Joseph 2013) .

The global references are available for comparison whereby the fetal growth ratio of ≥ 1.0 is considered as normals. Despite the availability of these reference values, lesser advantage has been taken from them. Although we dont find any local study for comparison but the slight degree of preponderance in fetal growth ratio among non-consanguineous new borne found in our study is also endorsed by an Indian study (Kuntla, Goli *et al.,* 2013) . Mayor & Joseph et al have also revealed the same findings (Mayer and Joseph 2013). The birth weight is also affected by parental inbreeding status & it may help the clinicians to predict adverse effect of consanguinity on birth weight (Balihallimath, Shirol *et al.,* 2015) . The consanguineous status may be written on the check lists of risk factors while filling the mother card in maternity wards. The multivariate analysis reveals parental inbreeding as an independent risk factor for delivering a baby with fetal growth ratio less than 1.0 (mean 0.859 ± 0.074 in both parents inbred as against 0.861 ± 0.104) in both parents non-inbred). The differences in effects of parental inbreeding were seen more remarkably at lesser gestational ages. We expect more significant results if we had conducted study on larger sample size. This finding of our study concurred with results of another research with similar objectives (Islam 2012). This finding throws light on the fact that gestational age is the strong confounder which needs invalidation while considering real associations between parental consanguinity & fetal growth ratio. Therefore a mixed-effect logistic regression model with 90.1% accuracy was applied to control various medical and socio-demographic expected covariates such as parity, maternal weight, socio-economic status, birth intervals etc. The odds for fetal growth ratio less than 1.0 was 1.48 (95% C.I 1.033 - 1.591; p=0.04) after adjusting for all the possible covariates. Similar were the findings in another study on Pakistani population revealing the odds for low fetal growth ratio in case of paternal inbreeding (Charafeddine, Ammous *et al.,* 2012).

Conclusions

Consanguineous marriage is the preferred pattern of marriage in our population. Parental inbreeding affects the birth weight of new borne at corresponding age of gestation & fetal growth ratio can be taken as the proxy measure for this purpose. This effect may be anticipated before searching for the cause of low birth weight of new borne among couples belonging to consanguinity of various degrees.

Disclaimer

This manuscript as well as its abstract has not been presented in any conference.

Declaration of No conflict of interest

There is no financial, personal or professional interest that could have influenced this work. The data is a part of the research work to fulfill the requirement for PhD in Epidemiology & Public health.

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