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RESEARCH ARTICLE

CONSANGUINITY: A RISK FACTOR FOR ADVERSE BIRTH OUTCOMES

***Dr. Khalida Naz Memon and Prof. Aneela Atta Ur Rahman**

Department of Community Medicine Liaquat University of Medical & Health Sciences, Jamshoro, Sindh, Pakistan

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ABSTRACT

Background & Objective: Marriages between close blood relations are extensively researched as being a risk factor for new borne but this aspect of research has not been done in our setup. The objective of this study was to determine the effect of consanguinity on birth come.

Methods: A comparative cross sectional study was conducted on 356 new borne delivered in various hospitals by filling a pre designed questionnaire. Intra uterine deaths, premature births & low Apgar score at birth were the selected variables for the study. The results were compiled through bivariate & logistic regression analysis.

Results: Among 203 new bornes of consanguineous parents, highest number was recorded for first cousins i.e. 99 (48.8%). In all, twenty four (6.7%) died intra utero, 38 (10.7%) were the premature, 64 (17.9%) had APGAR ≤ 6 at birth; five (1.4%) had no improvement at 5 minutes. Mean gestational age in consanguineous new borne was recorded as 38.15 ± 1.81 weeks as compared to 38.68 ± 1.11 weeks in non-consanguineous. Lowest gestational age at birth was observed among new bornes of uncle-niece relation i.e. 37.76 ± 2.02 weeks. Strong association was seen between consanguineous status & adverse birth outcome (p= 0.02); parental inbreeding revealed even more strong association (p=0.00). The odds of adverse birth oucome for consanguinity after incorporating other possible covariates, was 1.84 (95% CI= 1.56 - 8.905; p= 0.02).

Interpretation & Conclusion: Parental consanguinity is a risk factor for undesired birth outcome; however more rigorous studies with a large sample size separately incorporating adverse effects will be more conclusive.

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INTRODUCTION

Marriages between close blood relations have not been extensively researched as being a risk factor for undesired birth outcomes. From an operational point of view, union contracted between persons biologically related up to second cousins are categorized as consanguineous. These type of marriages are although viewed as objectionable but these are widely practiced & remain the choice of an estimated 10.4% of the global population (Bittles and Black, 2010). The estimates for consanguineous marriages range from 30-50% in Middle Eastern countries, 20-40% in Northern Africa & 10-20% in South Asia (Harkness and Khaled, 2014). In South Asian countries, even higher rates for cousin marriages have been reported (Joshi *et al*., 2009). In Pakistan, consanguineous marriage is practiced at high rate (Abbas and Yunis, 2014). These unions have been reported to be associated with high rates of adverse effects on the new borne (Abbas and Yunis, 2014). In Pakistan few studies to date have been conducted to document impacts of such marriages on new bornes' health (Rabbani and Qayyun, 2015). But we find no study no study which portrays the specific adverseeffect on new borne.This hospital based study has just provided an opportunity of performing a natural experiment in anatural environment to observe the effects of consanguinity on new bornes' health.

Study Hypothesis: Parental consanguinity is associated with adverse birth outcomes.

Objective: To determine the effect of consanguinity on birth outcomes.

MATERIALS AND METHODS

Cross-sectional data was collected through non-probability consecutive sampling technique through filling up of pre designed questionnaire on three hundred & fifty six consecutive live born singleton newborns delivered at theses public & private sector hospitals in Hyderabad. The questionnaire comprised of four sections having close ended questions. The new borne of age less than 48 hours fulfilling

Corresponding author: Dr. Khalida Naz Memon,
Department of Community Medicine Liaquat University of Medical & Health Sciences, Jamshoro, Sindh, Pakistan.

the eligibility criteria were the study subjects while their parents/ guardian were sources of information. The maternal obstetric history records & nursery charts were also used as support documents.

Study design

It was a hospital based comparative cross sectional study conducted in maternity wards of public & private sector hospitals in Hyderabad including Liaquat University Hospital Hyderabad & Jamshoro, CDF (Countess of Dufferin Hospital) Hyderabad, Wali Bhai Rajputana Hospital & jijal Maau Hospital Hyderabad. All the subjects fulfilling the eligibility criteria , reporting at specified hospitals for the study period of four months (from 1st October 2015 to 31st January 2016), were enrolled for the research through consecutive samplng technique.

Inclusion Criteria

1. New borne whose parents consented to be the part of the study.
2. Live borne, in utero dead as well as still borne.
3. Age ≤ 48 hours.
4. Gender: Both males & females.
5. Consanguinity upto 2nd degree blood relation.
6. New borne whose parents were in uncle-niece relation.
7. New borne of in-bred as well as out-bred parents.
8. Singleton births.
9. Term, pre-term & post-term new borne.
10. Intra uterine growth retarded babies.
11. Mode of delivery: Normal vaginal delivery & instrumental delivery including cesarean section.

Exclusion Criteria

1. New borne whose parents do not give permission to be the part of the study.
2. Age > 48 hours.
3. Consanguinity more than 2nd degree.
4. Twin babies.
5. New borne having any congenital abnormality.

Variables of Interest

Independent variable: Consanguinity upto second degree & uncle-niece relation, parental inbreeding.

Dependent variable: Adverse birth outcomes: Intr uterine deaths, still births, premature births & low Apgar score at birth, need for resuscitation at birth. 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.

Data analysis

After editing in MS Excel, the datawas entered & analyzed in SPSS version 16.0. The frequency of consanguinity was calculated as per hundred live births in all maternity wards. The frequencies of the categorical variables e.g. prematurity, still births, intrauterine deaths & need for resuscitation were calculated in percentages; their association with consanguinity was computed as Odd's ratios; bivariate analysis of categorical variables was followed by application of logistic regression. Means & standard deviations were computed for continuous variables eg gestational age & APGAR scores. After converting the continuous into categorical variables, logistic regression was applied to analyze the association of these variables with in-bred & out-bred groups of new bornes. The p-value of 0.05 was set as cut-off point for level of significance.

RESULTS

Among three hundred & fifty six subjects, two hundred & three (57%) were born to consanguineous parents, among them 99 (27.8%) were borne to first cousins, 83 (23.3%) to second cousins, 21 (5.9%) to uncle-niece relation. One hundred & fifty three (42.9%) were borne to non-consanguineous parents (Table I). Among total study subjects, there were 94 (26.4%) new borne whose both parents were inbred; 181 (50.8%) were borne to inbred fathers; 173 (48.6%) had mothers inbred (Table II). Overall 99 subjects (27.8%) had adverse birth outcomes (Chart I). Twenty four (6.7%) died intra utero, 38 (10.7%) were prematurely born, 63 (17.7%) had APGAR score of≤ 6at birthwho needed resuscitation; among them five (1.4%) had no improvement in APGAR at five minutes. The highest mean gestational age at birth was found in non-consanguineous new bornes i.e. 38.68 ± 1.11 weeks while lowest mean gestational age was recorded in those who were borne to uncle-niece relation (37.76 ±2.02) (Chart II & III). 64 (17.9%) had APGAR ≤ 6 at birth showing strong statistically significant association of low apgarr score at birth to new bornes consanguineous status & parental inbreeding (Chart IV & V) (Table III). Bivariate analysis for consanguineous status & adverse birth outcome showed strong statistical significance (p= 0.02); parental inbreeding revealed this association more strongly significant (p=0.00). Independently, first cousin marriage, father inbreeding, maternal inbreeding & both parents inbred were associated to adverse birth outcome with Odds ratios 1.12, 1.03, 1.10& 1.24 respectively (Table IV). The mixed model logistic regression analysis after incorporating other possible covariates revealed odds of adverse birth oucome for consanguinity as 1.84 (95% CI= 1.56 - 8.905; p= 0.02).

Table I. Consanguineous status of study subjects

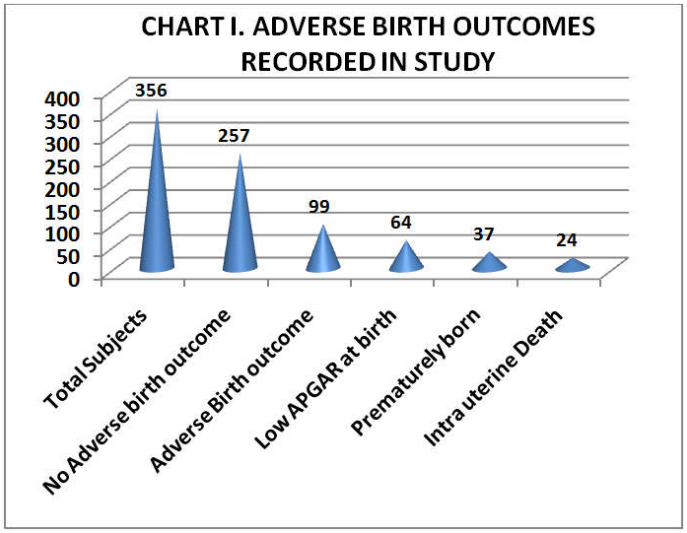
Consanguineous status	Frequency (%)
Consanguineous subjects (total)	203 (57%)
1st cousin	99 (27.8%)
2nd cousin	83 (23.3%)
Uncle-niece relation	21 (5.9%)
Non-consanguineous subjects (total)	153 (42.9%)

Table II. Parental inbreeding status of study subjects

Inbreeding status	Frequency (%)
Mother Inbred	173 (48.6%)
Father Inbred	181 (50.8%)
Both parents Inbred	94 (26.4%)
No parent Inbred	02 (0.56%)

DISCUSSION

Highest number of consanguineously borne children were the offsprings of first cousin marriages. Other studies also report the same findings that first cousine marriages are arround 20% & this trend has been stabilized at this level since last few decades (Ahmad *et al*., 2015).



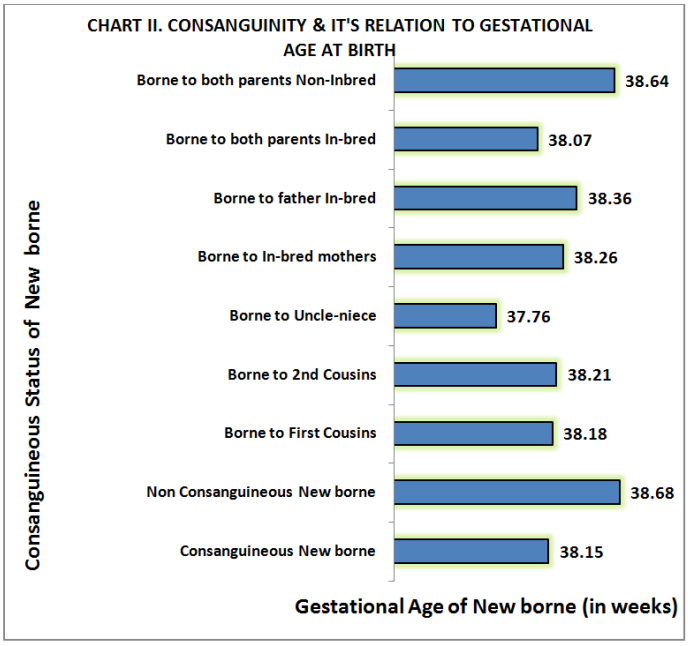
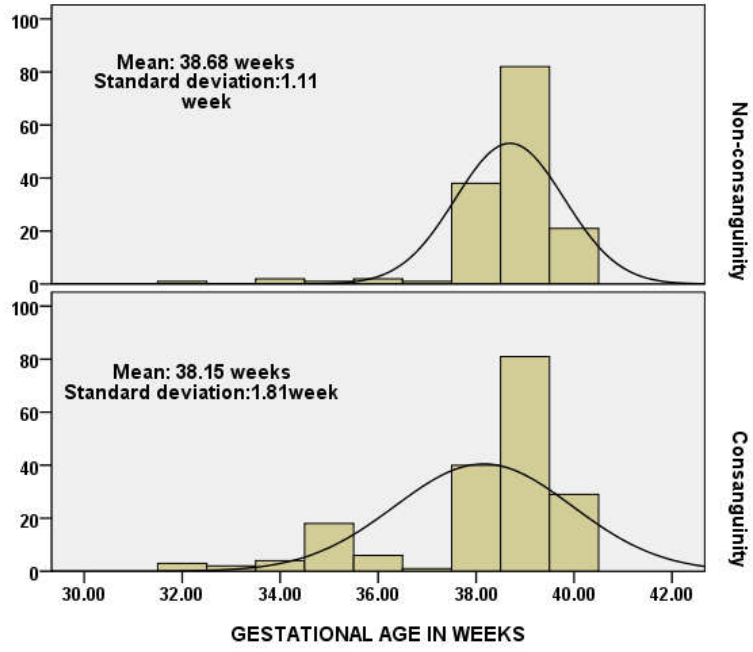
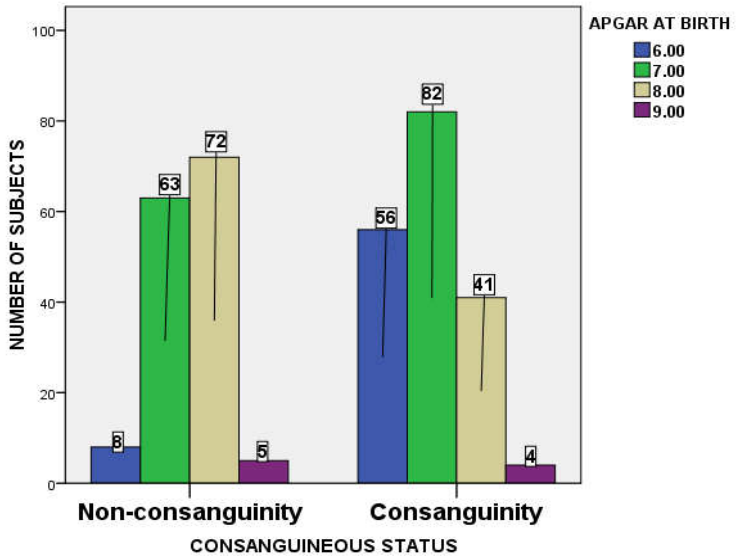


Chart III. Mean gestational age at birth consanguineous versus non-consanguineous new bornes



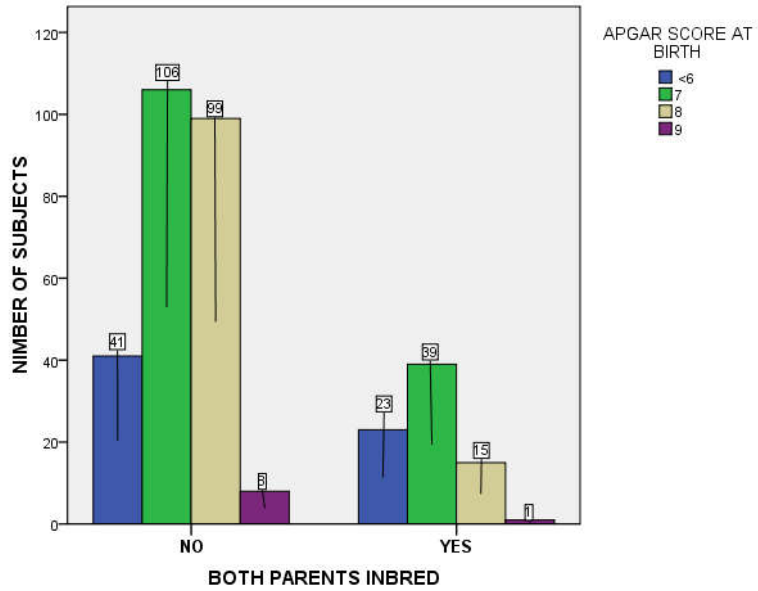
p =0.002

Chart IV. Distribution of low apgar scores among consanguineous & non-consanguineous new bornes



p =0.01

Chart V. Distribution of low apgar scores among parental in-bred & out-bred new bornes



p = 0.00

Table III. Association of various degrees of inbreeding withlow apgar scores at birth

Variables of Interest	Response	Apgar Score at Birth ≤ 6	Odds ratio	95% Confidence interval Lower-Upper	p-value
Consanguinity	Yes	74 (20.8%)	1.7	0.30 – 9.45	0.54
	No	13 (3.7%)			
Type of Consanguinity	1st cousin	38 (18.7%)	1.18	1.03 – 1.91	0.03
	2nd cousin	31(15.3%)			
	Uncle-niece	5 (2.5%)			
Father Inbred	Yes	58(16.3%)	1.54	0.51 – 4.65	0.44
	No	29 (8.2%)			
Mother Inbred	Yes	53 (14.9%)	1.95	0.65 – 5.89	0.23
	No	34 (9.6%)			
Both parents inbred	Yes	38(10.7%)	0.49	0.12 – 1.98	0.32
	No	49(13.8%)			

Table IV. Adverse birth outcomes in study subjects & their association to degree of consanguinity

Degree of consanguinity	Frequency (%)	Odd's ratio	95% confidence interval	P-value
1st Cousin Consanguinity	42 (42.4%)	1.12	1.05 - 2.69	0.031
Father Inbred	64 (35.4%)	1.03	1.04 - 2.56	0.027
Mother Inbred	59 (34.1%)	1.10	1.03 - 3.10	0.019
Both parents Inbred	42 (44.7%)	1.24	1.12 - 2.45	0.006

The authors also narrate that a substantioal rise has been observed in the inter caste marriages. This was also endorsed by other studies conducted throughout the world such as in Iran (Maghsoudlou *et al*., 2015) & China (Zhang *et al*., 2012). Concerning parental inbreeding, almost equal prevalence of paternal & maternal inbreeding was observed in the current study (48.6% against 50.8%). Parental single or double inbreeding is very commonly evidenced in various Asian countries (Saadat and Tajbakhsh, 2013). Parental inbreeding trends always encourage consanguineous marriages throughout the world (Biswas *et al*., 2016). Among total two hundred & three consanguineously borne babies, we find eighty four (41.8%) new bornes with adverse birth outcomes including intra uterine deaths, prematurely borne, low apgar scores at birth. One of the studies revealed that after adjusting the other possible risk factors for adverse birth outcomes, the intrauterine deaths & early neonatal deaths were the most commonly seen among offsprings of the consanguineous new bornes (Chaman *et al*., 2014). These findings are also endorsed by another study with similar objectives that perinatal mortality is more significantly associated with consanguinity (Maghsoudlou *et al*., 2015). Romeo G and Bittles AH also warned that closer inbreeding leads to twofold chances of intrauterine deaths (Romeo and Bittles, 2014). For this reason, Posch & Springer *et al* warrant the ante-natal counselling on this issue (Posch *et al*., 2012). Indirect evidence of the same findings were also revealed by Qandalji B whereby it was assumed that consanguinity has an adverse effect on pregnancy and neonatal outcome and should be considered as a factor in high risk pregnancy; the neonatologist and obstetricians should be alerted to such high risk pregnancies (Qandalji, 2012). This also opens a room for counselling services for future plans for marriages. The counselling services for such type of couples may have a positive impact on the future generations (Khan *et al*., 2010). We however find opposite opinions by few of other researchers who argue that being borne to consanguineous parents is not a major perinatal risk factor for tha new borne (Metgud *et al*., 2012; Metgud, Naik *et al*., 2012). The current study reveals that the non-consanguineous new bornes were delivered at slighthly more mean gestational age as compared to consanguineously borne babies. Moreover there was more variability in gestational ages at births in consanguineously borne babies in comparison to non-consanguineous babies.The variability in gestational age at birth & increased risk of being borne prematurely among consanguineously bornes was studied in details by Bellad & Gouder *et al.* (2012). Although the latter was a prospective study with a huge data but the results of this study are having gross similarity with the current study. Low gestational age at birth among consanguineous new bornes was found as a major risk factor for still births & early neonatal deaths (Chisholm and Bittles, 2015). It was also concluded in another study that consanguinity was closely linked to the preponderance of premature births in those countries where consanguinity was the cultural norm (Al-Mendalawi, 2014). In a study conducted in Lebonon, a close inverse relationship was revealed between inbreeding coefficient & prematurity at birth (El-Kheshen and Saadat, 2013). Consanguinity has been associated with healthy life at birth also (Saadat, 2011). The effect of consanguinity & parental breeding on APGAR score at birt has been rarely studied especialy in developing world; the reason behind this may be a long list of confounders related with this association.One of such rare studies, revealed strong association of inbreeding with low APGAR score at birth (Radfar *et al*., 2014). Similar were the findings of another research conducted in India (Metgud *et al*., 2012). We found in our study that 79.4% of the babies born with APGAR ≤ 6 were those who were prematurely borne. This invites a new research to seek association of consanguinity on APGAR score independent of gestational age at birth. We find odds of APGAR less than 6 at birth among offsprings of first cousins as 1.18 (95% CI = 1.03 -1-91, p= 0.03).

Conclusion

Parental consanguineous relation is a risk factor for undesired birth outcome.Prematurity is most commonly evident in parental uncle-niece relation & first cousin marriages are more frequently associated with low APGAR score at birth; however more rigorous study with a large sample size separately incorporating adverse effects & possible confounders will be more conclusive.

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