ORIGINAL RECEARCH ARTICLE

Association of consanguinity with neonatal asphyxia at birth: Evidence from Pakistan

DOI: 10.29063/ajrh2023/v27i7.8

Khalida Naz Memon[1], Zoheb Rafique Memon[1], Khalida Shaikh[2], Suhail Ahmed Bijarani[1], Urooj Bhatti[2] and Gulzar Usman[1]*

Department of Community Medicine & Public Health Sciences, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan[1]; department of physiology, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan[2]

***For Correspondence:** Email: *zoheb.memon83@gmail.com*; Phone: 92 0333 2756351

Abstract

Consanguinity commonly known as inbreeding is a state of offspring borne to couple sharing same ancestors. It is a least researched non-obstetric determinant of adverse birth outcome in developing countries like Pakistan. This hospital based study was designed to investigate the association between consanguineous status and neonatal asphyxia measured measured as low APGAR scores after birth in 879 newborns.The data regarding consanguineous status was obtained retrospectively. Potential covariates were incorporated for finding confounding effects. Data was analyzed in SPSS version 26.0 as mean ± standard deviation, unadjusted & adjusted odds ratios by logistic regression at P-values ≤ 0.05 significance for associations. Over 36.1% newborns were consanguineous, delivered with APGAR < 6 at 1-minute compared to 5.2% born to non-consanguineous parents. Premature birth was the single most important factor associated with neonatal asphyxia and low APGAR at 1 & 5-minute after birth. After adjusting for confounding variables, first cousin couples' offsprings showed OR of 9.1 & 4.1 for APGAR score ≤ 6 at 1 & 5-minutes after birth, respectively (P < 0.001 & P =0.001). We conclude that consanguinity is a strong determinant for neonatal asphyxia reported as low APGAR scores in this population of new borns. *(Afr J Reprod Health 2023; 27 [7]: 76-84).*

Keywords: Consanguinity, neonatal asphyxia, low APGAR, first cousin, second cousin inbreeding, uncle-niece inbreeding

La consanguinité communément appelée consanguinité est un état de progéniture né d'un couple partageant les mêmes ancêtres. C'est l'un des déterminants non obstétriques les moins étudiés de l'issue défavorable de la naissance dans les pays en développement comme le Pakistan. Cette étude en milieu hospitalier a été conçue pour étudier l'association entre le statut consanguin et l'asphyxie néonatale mesurée par des scores APGAR faibles après la naissance chez 879 nouveau-nés. Les données concernant le statut consanguin ont été obtenues rétrospectivement. Des covariables potentielles ont été incorporées pour trouver des effets de confusion. Les données ont été analysées dans SPSS version 26.0 en tant que moyenne ± écart type, rapports de cotes non ajustés et ajustés par régression logistique à des valeurs P ≤ 0,05 significativité pour les associations. Plus de 36,1 % des nouveau-nés étaient consanguins, nés avec un APGAR < 6 à 1 minute contre 5,2 % nés de parents non consanguins. La naissance prématurée était le facteur le plus important associé à l'asphyxie néonatale et à un faible APGAR à 1 et 5 minutes après la naissance. Après ajustement pour les variables confondantes, les descendants des couples de cousins germains ont montré un OR de 9,1 et 4,1 pour le score APGAR ≤ 6 à 1 et 5 minutes après la naissance, respectivement (P < 0,001 et P = 0,001). Nous concluons que la consanguinité est un déterminant important de l'asphyxie néonatale signalée comme de faibles scores APGAR dans cette population de nouveau-nés. *(Afr J Reprod Health 2023; 27 [7]: 76-84).*

Mots-clés: Consanguinité, asphyxie néonatale, faible APGAR, consanguinité germaine, cousine germaine, consanguinité oncle-nièce

Introduction

Consanguinity is a parallel terminology commonly used in place of inbreeding which is generally defined as marriage between close relatives[1]. This is reported with increased risk of adverse health effects[2]. Currently consanguinity is preferably practiced by over 10% of the global population[3]. In Pakistan, like other Asian countries, the rate of consanguineous marriage is even higher [4]. There is need to explore its multi dimensional impacts of on the new borns' health, especially at the time of birth. Neonatal asphyxia is considered as a potential cause of neonatal mortality world wide[5,6]. Globally neonatal asphyxia accounts for 24% of neonatal death annually[7]. This comprises of 31% of the total neonatal admissions and 21% of total neonatal mortality reported in hospitalized new

borns[8]. Neonatal asphyxia is a serious medical condition reported at a higher rate in consanguineous new borns[9]. A study found 19.8% of the cases of neonatal asphyxia as born to consanguineous parents[10]. However, this medical condition is preventable through early detection by APGAR scoring followed by proper neonatal resuscitaion. The APGAR scoring was introduced by Dr. Virginia Apgar in 1953 for rapid clinical assessment of the new born at 1-minute of age and thereby to do need assessment for prompt intervention for neonatal asphyxia[11]. It is considered to be the best available assessment tool for prediction of neonatal resuscitation[12]. This is especially meant for low resource settings, where more sophisticated methods of assessment of the condition of new borns in the very first critical minutes of life cannot be provided[13,14]. The APGAR score of 7-10 at one minute is considered as reassuring, 4-6 as moderately abnormal; while score 0-3 indicates a poor and compromised state of the new born health[15]. The correct use of APGAR scoring relates to its effective clinical predictive implications[16]. Authors suspect well established practice of consanguinity in Pakistan as underlying link to unpredicted genetic anomalies leading to neonatal asphyxia like musculoskeletal system anomalies eg. spina bifida, central nervous system anomalies like meningocoele, meningo myelocoele, cardiovascular system anomalies like patent ductus arteriosus, various septal defects as reported in other studies[17,18]. Studies show 20% higher risk of such congenital anomalies among neonates borne in consanguineous parental relations secondarily leading to neonatal asphxia owing to failure of new born to initiate and establish breathing due to incompetent respiratory system, cardiac dysfunction and central nervous system malfunctioning[18]. It has been extensively researched that APGAR score is greatly influenced by degree of immaturity of the newborn, so alone it cannot be considered as the evidence of any neurological insult to the newborn[19]. Some researchers contradict this opinion because not all components of APGAR scores correlated well with one another specially among pre-term infants[20]. The aim of this study was to evaluate the association between various degrees of consanguinity with neonatal asphyxia measures as APGAR score ≤ 6 at 1 and 5 minutes.

Consanguinity implies sharing of genetic heritage in limited natural gene selection. This results in higher probability of sharing of recessive genes in consanguineous newborns as compared to their non-consanguineous counterparts. The deleterious recessive gene expression may result in birth of new borns having genetic anomalies. Some of these anomalies like congenital heart defects, central nervous system anomalies, immaturity of respiratory system etc manifest as neonatal asphyxia. This results in failure of new born to initiate and maintain breathing at birth.

The low APGAR score at birth can be used as quick assessment method of neonatal asphyxia even before attempting to detect the specific underlying anomalies. The association of consanguinity with neonatal asphyxia can be seeked by comparing APGAR scores at 1 and 5 minutes among neonates borne to consanguineous & non-consanguineous groups after taking into account expected potential covariates.

Methods

Study population

A hospital-based retrospective study was conducted in Liaquat University of Medical and Health Sciences, Hyderabad and Jamshoro. A total of 879 data was collected during study period from June 2016 to March 2017. The new borns were examined within 48 hours after birth.

Participants' recruitment

The potential subjects i.e. new borns were recruited by convenient sampling after getting informed consent from the parents/guardians. The eligibility criteria for participants included all singletons born as non-consanguineous and consanguineous inclusive of those born to first cousins, second cousins and uncle-niece couples. The subjects were recruited irrespective of birth order, birth interval, gestational age at birth; the maternal age between 18-45 years for the current pregnancy was considered for participants recruitment. Twins were not recruited for study. Those born to

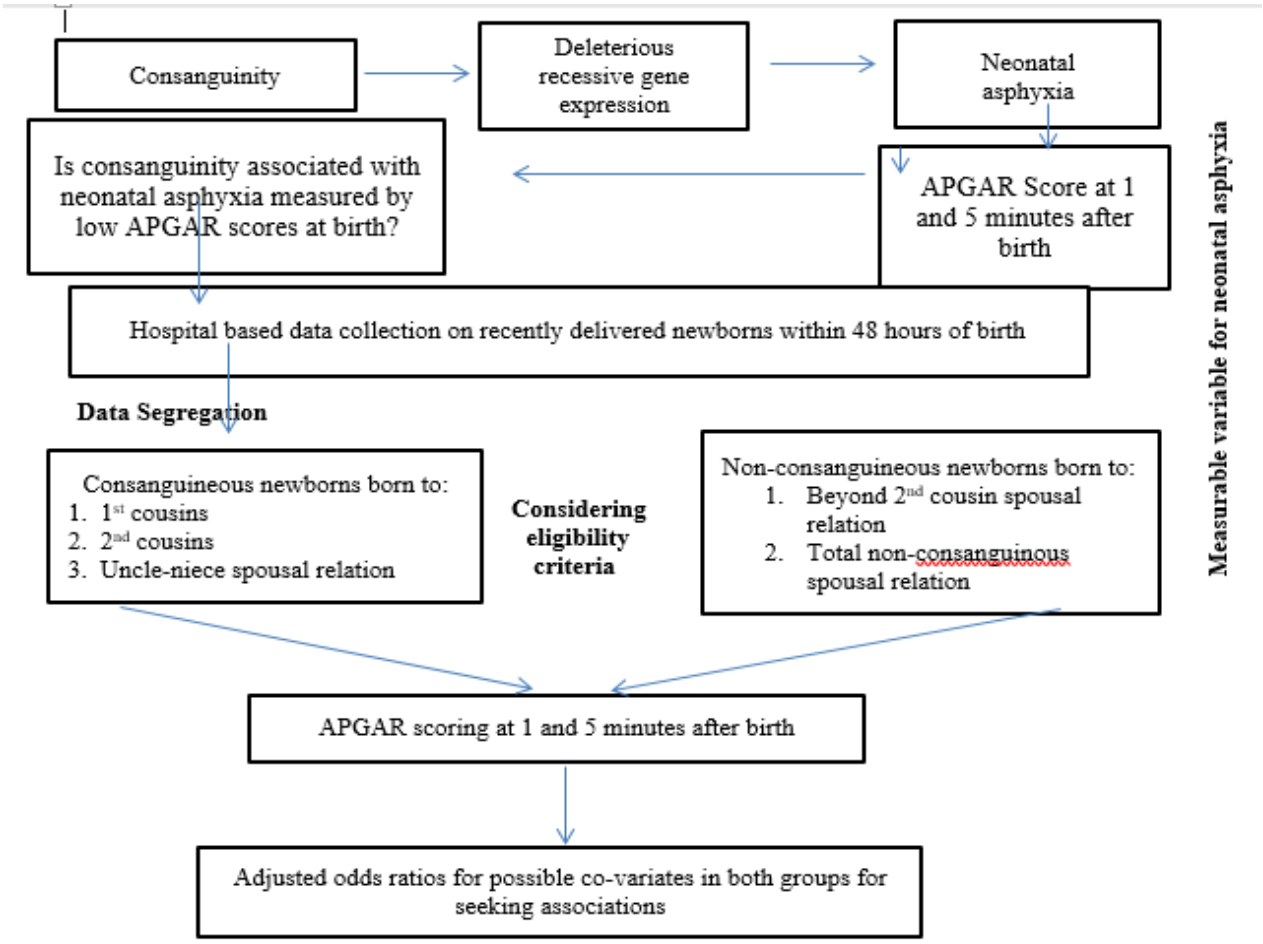

Figure 1: Conceptual Framework

mothers who had adverse obstetrical history in past were also excluded.

Definitions of independent and dependent variables and data retrieval

The neonates born to first cousin, second cousin and uncle-niece spousal relation were labelled as consanguineous group; the neonates born to any other spousal relation beyond second cousin were labelled as non-consanguineous group. Information regarding consanguinity was collected on a preformed questionairre available in local languages.

The cut-off APGAR score ≤ 6 at 1 and 5 minutes after birth was used as measurable parameter of identification of neonatal aspyxia in both groups of new borns. This tool is widely practiced in pediatrics wards for rapid assessment of neonatal asphyxia and its severity. This in turn facilitates in prompt initiation of resuscitation in those born with neonatal asphyxia. The conventional APGAR scoring method most commonly applied in hospitals comprises five components i.e. colour of skin, heart rate, reflex irritability, muscle tone and respiratory rate. Each of these is given a score of 0, 1 and 2. The 5 components incorporated in conventional APGAR scoring system are inter linked to assess the vital signs in new borns. The recording of findings on five-point scale was followed by summing up the five values at 1 and 5 minutes after birth to assess neonatal asphyxia in consanguineous and non-consanguineous groups of new borns.

The data was collected and documented in labor rooms of designated teriary hospitals. Besides this, the other sources of information included maternal obstetrical history record, new borns' medical record. The external birth defects

were recorded as per diagnosis by the attending physicians.

Ethical considerations

Prior to starting data collection, permission was obtained from Research Ethics Committee (REC), Liaquat University of Medical and Health Sciences and the authorities of the concerned hospitals. The Informed consent from couples was obtained. Maintenance of confidentiality of the record was ensured by keeping data under lock and key.

Data analysis

The 879 live born subjects were categorized into new borns with or without neonatal asphyxia based on priorly set cut-off APGAR score ≤ 6 at 1 and 5 minutes among various degrees of consanguinity. The cut-off point of APGAR ≤ 6 was selected because many studies endorsed possibility of new born survival at APGAR score > 6[11,14,15]. The SPSS software version 26.0 for windows was used for analysis. Mean and standard deviation of APGAR scores were calculated. The same were computed separately for term and pre-term new born. Bi-variate analysis was done to seek odds ratios (OR) for APGAR ≤ 6 at 1-minute for various confounders. The potential expected co-variates, e.g. prematurity, young age of mother (<25 years), high parity (birth order ≥ 3), vaginal mode of delivery, non-availing of ante-natal services (≤ 1), maternal illness, fetal malpresentation (other than cephalic) and external birth defects including overt anomalies were analyzed to seek their distribution in study subjects and their association with APGAR score ≤6 at 1 minute was determined. The overt anomalies along with external birth defects were least researched as covariates in the literature. To assess the risk of lesser APGAR scores (≤6) with the maternal and obstetric covariates, crude and adjusted ORs with corresponding 95% confidence intervals (CIs) were computed using bivariate and multivariate logistic regression. Significant associations of APGAR score ≤ 6 in bivariate analysis (with significance level of ≤ 0.05) were identified and were incorporated in the subsequently developed model of multivariate logistic regression. The independent predictors of low APGAR score were then determined.

While proceeding for segregated analysis in consanguineous group, the APGAR scores ≤ 6 at 1-minute was compared between first cousin offspring and reference group i.e. those parents who were related other than first cousin comprising of second cousins, uncle-niece relation. A sub-analysis was also performed to investigate odds of risk of being born with low APGAR scores separately among term and pre-term babies born to all degrees of consanguinity. The p-values ≤ 0.05 were considered statistically significant.

Results

Table 1 shows that there were 195 new born who were delivered with APGAR ≤ 6 at 1-minute after birth. Comparing consanguineous group of subjects to their non-consanguineous counterparts, the mean APGAR at birth was 6.8 ± 0.9 versus 7.6 ± 0.7 respectively. The difference of mean APGAR score at 1-minute after birth was significant among consanguineous group of subjects ($p<0.001$) and for those who were born to first cousins ($p=0.05$); while data revealed insignificant association between APGAR at 1-minute and second cousin spousal relation ($p=0.16$) as well as for uncle-niece relation ($p=0.36$). The 5-minute mean APGAR score among consanguineous and non-consanguineous group of subjects were calculated as 7.9 ± 0.7 and 8.4 ± 0.5 respectively. The bivariate analysis for difference in the mean APGAR scores at 5-minutes between both groups of new borns revealed significant association ($p<0.001$); while there were insignificant associations of APGAR score at 5-minutes for first cousin ($p=0.43$), second cousin ($p= 0.60$) and uncle-niece ($p=0.65$) spousal relations. Further analysis revealed the odds of APGAR ≤ 6 at 1-minute with significance level of ≤ 0.05 for prematurity (OR 13.7,95% CI 8.3 – 22.7, $P < 0.001$), maternal hypertensive disorders (OR 10.9, 95% CI 7.5 – 15.8, $P < 0.001$), non-availing of ante-natal care services (OR 2.0, 95% CI 1.2 – 3.4, $P < 0.01$) and vaginal mode of delivery (OR 1.5, 95% CI 1.1 – 2.2, $P < 0.01$) as covariates.

Table 2 depicts results for odds ratios adjusted for the potential covariates mentioned above. Here only first cousin spousal relation revealed statistically significant odds ratio of 9.1 to be at risk of being born with APGAR score ≤ 6 at

Table 1: Distribution of new born with APGAR score ≤ 6 at 1 and 5 minutes according to type of consanguinity

Groups of New borns	Frequencies	Frequencies of alive newborns with APGAR score ≤ 6 at 1- minute	1- minute APGAR scores Mean ± standard deviation (S.E)†	Frequencies of alive newborns with APGAR score ≤ 6 at 5- minute	5-minute APGAR scores Mean ± standard deviation (S.E)†
Consanguineous Group	481	174 (36.1%)	6.8±0.9 0.04)†	124 (25.7%)	7.9 ± 0.7 (0.03)†
Born to first cousin couples	221	82 (37.1%)	6.96 ± 1.0 (0.07)†	67 (30.3%)	7.9 ± 0.8 (0.05)†
Born to second cousin couples	211	77 (36.4%)	6.8 ± 0.9 (0.06)†	38 (18.0%)	7.9 ± 0.6 (0.04)†
Born to uncle-niece couples	49	15 (30.6%)	6.7 ± 0.8 (0.12)†	19 (38.7%)	7.9 ± 0.6 (0.08)†
Non-consanguineous Group	398	21 (5.2%)	7.6 ± 0.7 (0.03)†	09 2.2%)	8.4± 0.5 (0.02)†

† standard error for the mean APGAR score

Table 2: Distribution of new born with APGAR score ≤ 6 at 1 minute after birth according to type of consanguinity

Groups of New borns	Adjusted odds ratio	95% CI	P-values
Consanguineous Group	0.1	0.06 - 0.18	< 0.001
Born to first cousin couples	**9.1***	4.95 - 16.85	< 0.001
Born to second cousin	0.1	0.05 - 0.18	< 0.001
Born to uncle-niece couples	0.1	0.06 - 0.39	< 0.001
Non-consanguineous Group	0.1	0.02 - 0.11	0.023

***significant odds ratio**

Table 3: Distribution of new born with APGAR score ≤ 6 at 5 minute after birth according to type of consanguinity

Groups of New borns	Adjusted odds ratio	95% CI	P-values
Consanguineous Group	0.04	0.01 - 0.27	0.03
Born to first cousin couples	**4.1***	2.18 - 6.46	0.001
Born to second cousin couples	0.07	0.02 - 0.28	0.01
Born to uncle-niece couples	0.1	0.06 - 0.19	0.001
Non-consanguineous Group	0.09	0.05 - 0.18	0.01

***significant odds ratio**

Table 4: Association between type of consanguinity and APGAR ≤ 6 at 1- minute among pre-term and term live born

Groups of New borns	Pre-term live new born group			Term live new born group		
	Adjusted ORs	95% CI	P-values	Adjusted ORs	95% CI	P-values
Consanguineous Group	2.52	0.71 – 8.95	0.15	14.26	7.10 – 28.64	**< 0.001***
Born to first cousin couples	3.66	0.84 – 15.98	0.08	12.95	6.06 – 27.67	**< 0.001***
Born to second cousin couples	2.64	0.68 – 10.16	0.15	12.51	5.99 – 26.12	**< 0.001***
Born to uncle-niece couples	2.92	0.79 – 10.73	0.10	11.66	3.94 – 34.50	**< 0.001***

***significant odds ratio**

1 minute after birth. Table 3 shows the consistency of the same result with odds ratio of 4.1. Table 4 shows the association of 1-minute APGAR ≤ 6 separately among term and pre-term new born in various situations of consanguinity.

Discussion

The APGAR score a very easy tool to identify and measure the neonatal asphyxia uniformly at different obstetrical units throughout the world. Indirectly APGAR scoring assesses the quality of the perinatal and obstetrical care. The reason of this credit goes to its feasibility and cost-effectiveness. This scoring system was designed to help health care providers to assess newborn's physical condition and quickly decide whether the baby needed immediate medical care and referral and ultimately reduce the consequences of neonatal asphyxia.

There were in total eight hundred and seventy nine subjects born alive; among them one hundred and ninety five new born were delivered having APGAR score ≤6 at 1-minute i.e. 174 among consanguineous group while 21 in non-consanguineous group of subjects. At 5 minute after birth, this number reduced to 133 i.e. 124 in consanguineous group as compared to 9 in non-consanguineous group. This finding is supported by other studies, too[21,22]. The APGAR assessment within the first minute of birth is an indicator for intrapartum health and the neonatal response to any trauma of birth leading to neonatal asphyxia[23]. The same researchers emphasized that APGAR score assessment at 5-minute was a better predictor of neonatal asphyxia; therefore, a series of APGAR records would be more informative than a single APGAR record. The major referral hospitals in public sector were the study settings and these hospitals received high risk obstetric referrals. Therefore, this inevitably led to increased number of reported adverse pregnancy outcomes in terms of neonatal asphyxia reported as low APGAR scores at birth. This ultimately resulted in higher proportion of low APGAR scores reported in current study as compared to the national estimates. It was found eight times more frequent occurrence of low APGAR score among consanguineous new born as compared to their non-consanguineous counterparts. It was not only the high prevalence of lesser APGAR at birth, but the mean APGAR score among consanguineous group of subjects compared to their non-consanguineous counterparts i.e. 6.87±0.97 versus 7.65±0.73 respectively were also recorded. A study with similar objectives revealed consanguinity as an independent risk factor for lesser APGAR score at birth with a relative risk of 2.88 ($p<0.001$, 95% CI 1.98,4.18)[24]. The underlying covariates for neonatal asphyxia and low APGAR scores were however not delineated in this study. Another study found no such association; while the mean APGAR scores in all births were calculated as 8.50 ± 1.40[25]. The APGAR score at 5-minute is considered as an important predictor of neonatal survival and the scores ≤ 3 revealed the highest relative risk of neonatal death as compared to scores ≥ 3[26].

The results from a study, comprising of large number of newly born subjects, showed an association between an APGAR score less than ≤ 6 at 5-minutes after birth and parental consanguineous status[27]. This was in contrast to 195 new born having APGAR scores ≤ 6 at 1-minute after birth. There were only 18(1.90%) neonates having APGAR ≤ 6 at 5-minutes; among them 17 belonged to consanguineous group; while only one subject belonged to the non-consanguineous group. The mean APGAR scores at 5 minutes were 7.96 ± 0.73 and 8.49 ± 0.54 for both these groups respectively.

The consanguineous marriage pattern was reported as a significant predictor for neonatal asphyxia and low APGAR score at 5-minute in studies by other researchers, too[28,29]. An APGAR score ≤ 6 is an alarm to bad prognosis for future health status of the new born; however, it may be the indicator of a variety of underlying factors. This necessitates sorting out confounders while seeking such associations. Prematurity was found as the strongest predictor for lesser APGAR score at birth. The intrinsic physiological immaturity and inadequate capacity to respond to an altered physiological environment is reflected as neonatal asphyxia and low APGAR scores in prematurely born babies. Many studies found prematurity as the most evident risk factor for lesser APGAR scores at 1 and 5 minutes (OR 8.0; 95% CI 5,12; $p<0.001$)[30]; the same were the findings in current study too. However, regarding gestational age, a minimum threshold for inclusion was set as ≤ 37 weeks which was higher as compared to other

studies, which incorporated even gestational age less than 32 weeks. Regarding maternal hypertensive disorders including preeclampsia, although literature does not support the higher rate of occurrence of pre-eclampsia among consanguineous spousal unions, but it is a well-established fact that pre-eclampsia results in preterm delivery which is one of the strongest predictors of neonatal asphyxia and low APGAR score at birth[31]. Current study revealed the vaginal mode of delivery as being 1.59 times more associated with neonatal asphyxia and lowered APGAR scores at birth (OR= 1.59; 95% CI: 1.15, 2.22; p<0.01). Similar to these findings, the elective CS was associated with odds of recovery from neonatal asphyxia 2.70 times greater than uncomplicated vaginal deliveries (95% CI: 1.39–5.23); and emergency CS was associated with 1.70 times greater odds of recovery (95% CI: 1.23–2.37) [23]. Similarly, the effective strategies of health education are, therefore, imperative to improve access to ante-natal care services especially in the vulnerable group of population, i.e. consanguineous group because the under-attendance at antenatal care services carries a substantially higher risk of severe adverse pregnancy outcome. Exploring the adjusted odds ratios, a positive association between first degree consanguinity and low APGAR score at birth in current study (OR 9.14; 95% CI 4.95,16.85; p<0.001) was similar with the results of the other studies[9,32]. Surprisingly, the significant positive association did not consistently remain when consanguineous status was bifurcated to second cousin or uncle-niece spousal relation. However, comparing new born of first cousins to those born to non-consanguineous parents, the risk of neonatal asphyxia with APGAR score ≤ 6 at 1-minute was raised to 11.30 (95% CI 5.06, 18.78; p=0.01). These risks among newborns of second cousins and of uncle-niece spousal relation compared to non-consanguineous parents were 0.12 (95% CI 0.08, 0.19; p=0.01) and 0.38 (95% CI 0.17, 0.69; p=0.01) respectively. For finding the preterm birth as risk factor for neonatal asphyxia and lesser APGAR score at birth, separate sub-analyses of lesser APGAR score among pre-term and term babies were also done. Among total 195 study subjects, 35.38% belonged to pre-term group; while 64.62% belonged to term new born. Segregated analysis seeking association between consanguinity and low APGAR score separately among pre-term and term new born revealed entirely different results i.e. OR 2.52 (95% CI 0.71, 8.95; p=0.15) in preterm and term babies (OR 14.26; 95% CI 7.10, 28.64; p<0.001) respectively. This highlights the impact of prematurity on lowering the APGAR at birth. However, no such study was found to compare the results. This emphasizes the need of such type of research stratifying the gestational age while seeking association with APGAR scores. In term babies, the study highlighted the role of co-variates in determining the 1-minute APGAR score at birth in all degrees of consanguinity.

Conclusion

The study highlighted the association of consanguinity to neonatal asphyxia and in low recorded APGAR scores which can lead to undesired health impacts on the new born; among multiple co-risk factors, prematurity was one of the strong predictors for low APGAR score at birth. However, there was lack of comprehensive research on various degrees of consanguinity and its effects on neonatal asphyxia to compare with the present results. Communities should be informed specifically regarding hazardous effects of consanguinity on health of neonates especially in society where custom of intra family marriage is common. Furthermore, broad-based, prospective etiologic studies should be conducted to verify these findings. The study also suggests for concerted effort to identify families at increased risk, and to provide them risk information, awareness regarding carrier testing and neonatal health monitoring when feasible.

Acknowledgements

The authors acknowledge the administration of concerned hospitals for granting permission for data collection. The kind cooperation of parents of study subjects is also acknowledged by authors.

Competing interests and funding

The authors declare that they have no competing interests. Moreover, this was a non-funded research.

Availability of data

The data set used in current study is available from the corresponding author on reasonable request.

References

1. Gamella JF. Consanguineous marriages among Andalusian Gitanos/Calé: A genealogical analysis (1925–2006). Journal of Biosocial Science. 2020; 52(6): 809-31.
2. Anwar S, Taslem M J, Arafat Y, Hosen MJ. Genetic and reproductive consequences of consanguineous marriage in Bangladesh. PloS One. 2020; 15(11): e0241610.
3. Oniya O, Neves K, Ahmed B and Konje JC. A Review of the Reproductive Consequences of Consanguinity. Eur J Obstet Gynaecol and Repro Biol. 2019; 23(2):87-96.
4. Hasan ST, Safdar S and Afzal A. Parents Knowledge and Attitude regarding Consanguineous Marriage and its impact on Child health: A study of district Gujranwala, Punjab, Pakistan. Int J Speci Edu. 2022; 37(3): 101-07.
5. Abubakari A, Taabia FZ and Ali Z. Maternal determinants of low birth weight and neonatal asphyxia in the Upper West region of Ghana. Midwifery. 2019; 73:1-7.
6. Collins KA and Popek E: Birth injury: Birth asphyxia and birth trauma . Acad Forensic Pathol. 2018, 8: 788-864. 10.1177/1925362118821468.
7. Berhe YZ, Kebedom AG, Gebregziabher L, Assefa NE, Berhe LZ, Mohammednur SA et al. Risk factors of birth asphyxia among neonates born in public hospitals of Tigray, Northern Ethiopia. Pediatric health, medicine and therapeutics. 2020; 8: 13-20.
8. Camara B, Oluwalana C, Miyahara R, Lush A, Kampmann B, Manneh K, Okomo U, D'Alessandro U and Roca A. Stillbirths, neonatal morbidity, and mortality in health-facility deliveries in urban Gambia. Frontiers in Pediatrics. 2021;9: 579922.
9. Choudhry A, Habib M, Shamem Z, Batool SZ, Barkat S, Naseem M and Nisar S. Effects of consanguineous marriages on perinatal outcome. Pak Armed Forces Med J 2020; 70 (3): 727-33.
10. Gumus H and Demir A. An evaluation of risk factors in cases of perinatal asphyxia. J Clin Exp Invest. 2021;12(1): 343-51.
11. Uhl XM and Apel MA. Virginia Apgar: Groundbreaking Doctor. The Rosen Publishing Group, Inc; 2019; 15: 314-28.
12. Niemuth M, Küster H, Simma B, Rozycki H, Rüdiger M and Solevåg AL. A Critical Appraisal of Tools for Delivery Room Assessment of the Newborn Infant. Pediat Res 2021; 30:1-7.
13. Tylleskär T, Cavallin F, Höök SM, Pejovic NJ, Lubulwa C, Byamugisha J, Nankunda J and Trevisanuto D. Outcome of Infants with 10 min APGAR Scores of 0–1 in a Low-Resource Setting. Arch Dis in Childhood - Fetal and Neonatal Edition 2022;107(4):421-4.
14. Chiabi A, Kago DA, Moyo GP and Obadeyi B. Relevance and Applicability of the Apgar Score in Current Clinical Practice. EC Paediatrics 2019; 8(11): 01-7.
15. Michel A and Harris-Haman PA. Review of the Reliability and Validity of the APGAR Score. Advances in Neonatal Care 2022; 22(1): 28-34.
16. Bovbjerg ML, Dissanayake MV, Cheyney M, Brown J and Snowden JM. Utility of the 5-minute APGAR Score as a Research Endpoint. Am J Epidemiol 2019; 188(9): 1695-704.
17. Sinha A, Tripathi S, Nigam N, Kumar M and Singh SN. Profile of neonates born with congenital birth defects in a tertiary care hospital of North India: An observational study. Clinical Epidemiology and Global Health. 2022; 14: 100999.
18. Al-Joborae SF, al-Sadik ER, Al-Humairi AK, Al-Joborae HFand Hussein AM. A Study of the Association of Parental Consanguinity with Birth Defects and Neonatal Medical Problems in Babylon Province. Journal of University of Babylon, Pure and Applied Sciences. 2018; 26(6): 53-143.
19. Silva MM, Brito AL, Vasconcelos IÁ, Souto RE, Rocha RP, Esteche CM, Damasceno AK, Moraes JL and Saraiva MR. Profile of women affected with Premature Childbirth and Neonatal Outcomes. Revista Brasileira de Saúde Materno Infantil 2022; 21: 979-86.
20. Abukari AS, Awuni N, Yakubu I, Mohammed S, Yakubu A and Yakubu S. Factors Associated with Low Fifth Minute APGAR Score in Term and Preterm Singleton Live Births in a Ghanaian Hospital. J Neo Nurs 2021; 27(6): 476-82.
21. Khatibi T, Farahani A, Sepehri MM and Heidarzadeh M. Distributed Big Data Analytics Method for the Early Prediction of the Neonatal 5-Minute APGAR Score Before or During Birth and Ranking the Risk Factors from a National Dataset 2022; 3(2): 371-89.
22. Zaman N, Mumtaz H, Zafar A, Rehman HM, Sohail A, Ahmad S and Ahad SA. Incidence of Asphyxia Neonatorum with Complications at a Specialized Medical Care Hospital. J The Soc of Obstet and Gynaecol of Pakistan 2022; 12(3) : 199-213.
23. Jeganathan R, Karalasingam SD, Hussein J, Allotey P and Reidpath DD. Factors Associated with Recovery from 1 Minute APGAR Score < 4 in Live, Singleton, Term Births: An Analysis of Malaysian National Obstetrics Registry Data 2010– 2012. BMC Pregnancy and Childbirth 2017; 17(1): 1-2.
24. Kapurubandara S, Melov S, Shalou E and Alahakoon I. Consanguinity and Associated Perinatal Outcomes, Including Stillbirth. Australian and New Zealand J Obstet and Gynaecol 2016; 56(6): 599-604.
25. Islam MM, Al-Thihli K and Abdellatif M. Maternal and Neonatal Factors Influencing Preterm Birth and Low Birth Weight in Oman: A Hospital Based Study. Inter J Child Health Nutr 2013; 2: 281-95.
26. Tavares VB, Affonso MV, Da Rocha ES, Rodrigues LF, da Costa Moraes LD and dos Santos Coelho GC et al. Factors associated with 5-min APGAR Score, Death and Survival in Neonatal Intensive Care: A Case-Control Study. BMC Pediat 2022; 22(1): 1-10.

27. Getachew B, Etefa T, Asefa A, Terefe B and Dereje D. Determinants of Low Fifth Minute APGAR Score Among Newborn Delivered in Jimma University Medical Center, Southwest Ethiopia. Inter J Pediat 2020; 4(1): 1-7.
28. Tanous O, Watad M, Felszer-Fisch C, Peniakov M, Miron D and Salim R. Risk Factors for Mortality Among Newborns with Neonatal Seizures. Neuropediat 2021; 52(02): 84-91.
29. Killion MM. Correct Use of the APGAR Score. MCN: The Am J Mat Child Nursng 2016; 41(2): 123.
30. Lai S, Flatley C and Kumar S. Perinatal Risk Factors for Low and Moderate Five-Minute APGAR Scores at Term. Euro J Obstet , Gynecol and Rep Biol 2017; 210:251-6.
31. Sirenden H, Sunarno I, Arsyad MA and Idris I. Birth Weight, APGAR Score and Fetal Complications in Mothers with Severe Preeclampsia. Enfermeria Clinica 2020; 30(1): 533-6.
32. Teebi AS and El-Shanti HI. Consanguinity: implications for practice, research, and policy. Lancet 2006; 367(9515): 970–71.