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Prevalence of birth abnormalities and congenital malformations in progenies from parental consanguinity in Rajshahi City Corporation area, Bangladesh

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Abstract

In a series of two separate studies during January through August 2018, various birth abnormalities (BA) from 178 clinical cases and congenital malformations (CMF) from 70 consanguineous marriages (CM) and 100 non-consanguineous marriages (NCM) within the Rajshahi City Corporation (RCC) area have been recorded, analyzed and interpreted. Results demonstrate that frequencies of miscarriages (5.69 *vs.* 3.00), stillbirths (3.85 *vs.* 1.00), postnatal deaths (8.97 *vs.* 1.00), preterm deliveries (29.49 *vs.* 38.00) and breech births (6.41 *vs.* 4.00) were significantly greater in CM compared to the NCM counterparts. In addition, both gestational ages and live birth weights of the children from CM were significantly lesser than those recorded from the NCM couples. Of 205 children derived from 70 CM couples 67 were suffering from various CMF, the remaining 138 children were normal. Compared to this, only 2 out of 267 children were affected from 100 NCM couples. Mental retardation (MR) represented the highest CMF (n= 37), followed by cerebral palsy (CP; n= 16), crossed-eyes (CE; n=4), blindness (BL) and microcephaly (MC; n= 3 each), deaf-mute (DM; n= 2), and Down's syndrome (DS) and syndactyly (SD; n= 1 each). In contrast to the CM cases, the NCM couples had only two affected children, one crossed-eyed girl and the other polydactylous boy. The overall frequency of CMF in CM (32.68) was much higher than that in NCM cases (0.75). In relation to parental consanguinity, the importance of genetic counselling and pre-implantation screening relevant to the present findings has been emphasized in this report.

Key words: Parental consanguinity, birth abnormalities, congenital malformations.

INTRODUCTION

Marriages between 'bloods relatives' *i.e.* between persons who have one or more common ancestors are known as consanguineous marriages (CM), which are usually marriages between first cousins (Emery & Mueller, 1992). Since cousins have one or both grandparents in common and if either of the two grandparents, maternal or paternal, carries a defective recessive gene, it stands a good chance of becoming homozygous in any one child who is a product of such CM (Novitski, 1977). Congenital malformations (CMF), on the other hand, refer to any abnormalities, whether genetic or environmental, which are present at birth and which represent one of the major childhood health problems in children from consanguineous parents (Saggara & Bittles, 2008; Tayebi *et al.*, 2010). The most common CMF include cleft lips, cleft palates, club feet,

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microcephaly, blindness, deaf-mutism, mental retardations, polydactyly and other abnormalities of the limbs (Søgaard & Vedsted-Jakobsen, 2003). According to a recent estimate, approximately 6% of births worldwide, 7.9 million children, are born with serious CMF each year (Ng, 2016). Despite some perceived benefits of CM like preservation of tradition, stronger family ties, financial advantages, and bride protection, the potential harms of CM such as autosomal recessive disorders, complex CMF, stillbirths and postnatal mortality are obvious from various studies (Barrett, 2016).

Previous reports show that consanguinity increases the probability of detrimentally affected offspring in the population. Examples include pre- and postnatal deaths in babies from first cousin marriages (Morton, 1961), hearing impairment and deaf-mutism (Ben Arab *et al*., 1990) and blindness (Elder and De Cock, 1993). Children of consanguineous parents may be over represented in patients with severe mental retardation (Al-Hakeem & Hamamy, 1992; Bener *et al*., 2007). Substantially high proportions of recessively inherited mental and physical handicapped children resulted from CM in Iraq (Al-Hakeem & Hamamy, 1992) and over 80% single gene autosomal recessive disorders and 22% CMF were recorded among 16,419 births in Saudi Arabia (Al-Abdulkareem & Ballal, 1998). Consanguinity associated deaths are largely concentrated during the first-year of children's life (Hussain *et al*., 2001). Moreover, reports indicate that morbidity levels of the progeny of first cousins are 1-4% higher than in the offspring of unrelated couples (Bittles, 2002) and CM lead to an increased birth prevalence of infants with severe recessive disorders (Modell & Darr, 2002). Online literature searches on the incidence and consequences of CM in India (Badaruddoza & Akhtaruzzaman, 2007), Qatar (Bener *et al*., 2007), Lebanon (Ghina *et al*., 2007), Tunisia (Kerkeni *et al*., 2007), Jordan (Obeidat *et al*., 2008), North Africa, the Middle East and large parts of Asia (Saggara & Bittles, 2008), Morocco (Jaouad *et al*., 2009), Kuwait (Al-Kandar & Crews, 2011), for the people of Pakistani origin in the UK (Chinthapalli, 2013; Bittles, 2013), for Arabs in Israel (Na'amnih *et al*., 2015), Turkey (Wong, 2015) and overall world's population (Oniya *et al*., 2019) have been conducted for comparison with the present results.

In recent years, genetic counselling has come to be considered in health care services. Data obtained through genetic counselling offered during a 5-year period in Isfahan, Iran that has a high rate of CM, for example, revealed that 74.3% had consanguineous relationships, 62.3% were first cousins, 1% double cousins and 7.8% second cousins (Nouri *et al*., 2017). Because CM are still nowadays widely acceptable in our society in Bangladesh, the role of public health professionals and primary care personnel is to provide comprehensive information about the potential genetic risks of consanguinity on offspring health and also to increase the accessibility of premarital and preconception

counselling services. This led to design the present investigation, the major aims of which were: (a) to estimate the prevalence of birth abnormalities (BA) and CMF from progenies of parental consanguinity in the selected clinical samples as well as from offspring of CM within the Rajshahi City Corporation (RCC) area; (b) to compare the prevalence of CMF between CM and NCM cases; and (c) to recommend premarital and preconception counselling on the harmful consequences of parental consanguinity for the prospective couples, particularly in the rural and semi-urban populations under study.

MATERIALS AND METHODS

Experimental design: Structured questionnaires designed by Hamamy (2012), Shawky *et al*. (2013) and Teeuw *et al*. (2014) with slight modifications as required were used to collect data on CM and non-CM cases, along with various BA and CMF within the RCC area, Bangladesh. The present research was split into two consecutive studies described below.

Study 1: This part of the research involved 178 clinical cases within the RCC area to study various BA in CM and NCM couples. Data were collected from Rajshahi Medical College Hospital (RMCH) and 10 selected private clinics situated in the RCC area (Table 1). To maintain the privacy of the clinics and that of the patients, however, no names and addresses are mentioned in the report. The study was conducted from January to June 2018.

Table 1. Numbers of consanguineous couples and their parental consanguinity *versus* numbers of non-consanguineous couples used for recording birth defects in the newborn babies from the RCC area, Bangladesh

Parental consanguinities	N	Consanguineous couples	N	Non-consanguineous couples	N
Paternal cousins	24	From private clinics (n=10)	38	From private clinics (n=10)	50
Maternal cousins	28	RMCH Pediatrics Ward	10	RMCH Pediatrics Ward	15
Bi-parental cousins	26	RMCH Gynecological Ward	26	RMCH Gynecological Ward	15
		RMCH General Ward	4	RMCH General Ward	20
Total	78		78	Total	100

Study 2: Here the effects of parental consanguinity on different CMF were studied from 70 CM and 100 NCM families within the RCC area (Table 2). The study was conducted from March to August 2018.

Table 2. Numbers of consanguineous couples (n=70) and their parental consanguinities *versus* numbers of non-consanguineous couples (n=100) used for recording various CMF in the newborn babies from the RCC area, Bangladesh

Consanguineous couples	N	Non-consanguineous couples	N
Paternal cousins	30		
Maternal cousins	22	Unrelated Males × Females	100
Bi-parental cousins	18		
Total	7 0		100

Birth abnormalities (BA): The following five birth abnormalities *viz*., miscarriages (spontaneous abortions), stillbirths, postnatal deaths, preterm deliveries and breech births were recorded from 178 clinical cases. In addition, gestational ages (weeks) and live birth weights (Kg) were also noted for the newborn babies.

Congenital malformations (CMF): A total of 14 CMFs were recorded in the offspring from CM and NCM couples under study. These include: abnormal voice, blindness, cerebral palsy, cleft lip, crossed-eyes, deaf-mute, Down's syndrome, dwarf, mental retardation, microcephaly, non-articulated speech, polydactyly, postnatal death and syndactyly.

Statistical analyses: Experimental data on BA and CMF were collected in survey sheets designed for this investigation. All couples/mothers were interviewed separately for recoding their histories. Photographs of some CMF children were taken with their parents' permission. The data were subjected to either chi-square or Student's t-tests as appropriate, and were analyzed using SPSS (version 11.5) for Windows.

RESULTS AND DISCUSSION

Birth abnormalities (BA): Effects of CM *versus* NCM on some BA recorded from 178 clinical cases within the RCC area are presented in Table 3. Results demonstrate that frequencies of miscarriages (5.69 *vs.* 3.00), stillbirths (3.85 *vs.* 1.00), postnatal deaths (8.97 *vs.* 1.00), preterm deliveries (29.49 *vs.* 38.00) and breech births (6.41 *vs.* 4.00) were significantly greater in CM compared to the NCM counterparts (Table 3; t-values values; $P<0.05$-$P<0.001$). Moreover, both gestational ages ($t= 6.18$; $P<0.001$) and live birth weights ($t= 2.48$; $P<0.05$) of the children from CM were significantly lesser than those recorded from the NCM couples (Fig. 1).

An early study by Morton (1958) in American population showed that birth defects owing to consanguinity include stillbirths and neonatal deaths (0.111%) and infant and juvenile

deaths (0.156%). In addition, increased proportions of pre- and postnatal deaths (6% greater in each) in babies from first cousin marriages were recorded (Morton, 1961). Hussain *et al*. (2001) noted consanguinity associated postnatal deaths in the first year of life in Muslim children from India and Pakistan. Multinational studies of over 600,000 pregnancies and live births in 10 populations from India (Bittles *et al.*, 1991; Bittles & Neel, 1994; Bittles, 2002, 2003) show that postnatal deaths in 6 months to 10 year-old progenies from CM were 4.4% higher.

Table 3. Birth abnormalities (BA) associated with consanguineous (CM) and non-consanguineous (NCM) couples recorded from 178 clinical cases within the RCC area, Bangladesh

Birth abnormalities (BA)	CM (n=78)	NCM (n=100)	t-test values	Probabilities (P)
Miscarriages	6 (5.69)	3 (3.00)	8.14	P<0.001
Stillbirths	3 (3.85)	1 (1.00)	2.15	P<0.05
Postnatal deaths	7 (8.97)	1 (1.00)	14.18	P<0.001
Preterm deliveries	23 (29.49)	38 (38.00)	2.52	P<0.05
Normal deliveries	34 (43.59)	53 (53.00)	8.25	P<0.001
Breech births	5 (6.41)	4 (4.00)	2.07	P<0.05
Gestational ages (wk)	34.52±3.18	39.01±3.02	6.18	P<0.001
Live birth weights (kg)	3.33±1.07	4.16±0.98	2.48	P<0.05

CM= consanguineous marriages; NCM= non-consanguineous marriages; all t-values are at 176 df.

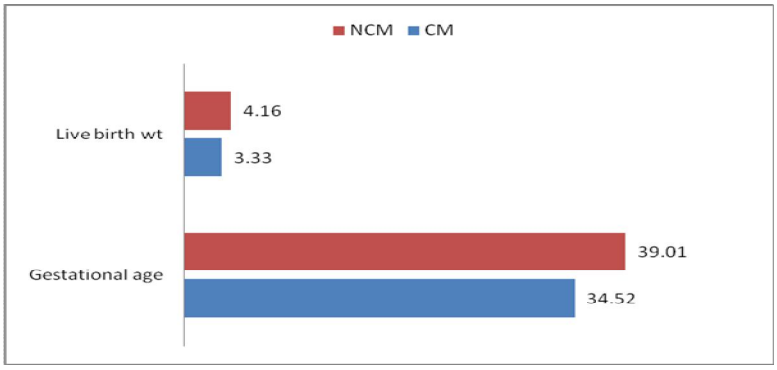

Fig. 1. Gestational ages (weeks) and live birth weights (kg) from consanguineous (CM) and non-consanguineous (NCM) newborn babies within the RCC area, Bangladesh

Another study by Kerkeni *et al.* (2007) revealed that spontaneous abortions, stillbirths, and neo- and postnatal deaths of children under 5 were significantly higher in CM in Tunisia. These findings corroborate to our results. Similar to the present data, Morton (1958) found shorter gestation length (<40.13 wks) and Obeidat *et al*. (2008) recorded 12.3% preterm delivery in consanguineous cases. Moreover, reports indicate that

significantly lighter birth weights in live born babies [3.046 kg in America (Morton, 1958); 1.8% less in Lebanon (Ghina *et al.*, 2007) and 10.1% low in Jordan (Obeidat *et al.*, 2008)] are common due to consanguinity. The present results clearly indicate the detrimental effects of marriages between close relatives on different BA and CMF cases in the study area.

Congenital malformations (CMF): Of 205 children (1♂: 1.18♀) derived from 70 consanguineous couples, 67 (21 boys and 46 girls; 1♂: 2.19♀) were suffering from various CMF, the remaining 138 children were normal (Table 4). Compared to this, only 2 (1 boy and 1 girl; 1♂: 1♀) out of 267 (138 boys and 129 girls; 1♂: 0.94♀) children were affected from 100 non-consanguineous couples. It therefore appeared from the present study that a greater number of girls were affected by their parental consanguinity.

Table 4. Number of congenitally malformed children from various parental consanguinities compared to non-consanguineous marriages within the RCC area, Bangladesh

Parental consanguinities	No. children			Non-consanguineous couples	No. children		
	Affected	Normal	Total		Affected	Normal	Total
Paternal cousins (n=30)	36	48	84				
Maternal cousins (n=22)	20	52	72	100	2	265	267
Bi-parental cousins (n=18)	11	38	49				
Total= 70	67	138	205	Total= 100	2	265	267

In the present study, eight CMF were recognized from 67 affected children (Table 5; Plates 1-6). Of these, 30 came from paternal, 22 from maternal and 11 from bi- parental cousin marriages. Mental retardation (MR) represented the highest CMF (n= 37), followed by cerebral palsy (CP; n= 16), crossed-eyes (CE; n=4), blindness (BL) and microcephaly (MC; n= 3 each), deaf-mute (DM; n= 2), and Down's syndrome (DS) and syndactyly (SD; n= 1 each). However, 73 normal males and 65 normal females were also produced by 70 consanguineous couples under study. In contrast to the CM, the non-consanguineous couples had only two affected children, one crossed-eyed girl and one polydactylous boy. The overall frequency of CMF in CM (32.68) was much higher than that in NCM cases (0.75).

Table 5. Frequencies of various congenital malformations (CMF) from 70 consanguineous couples and 100 non-consanguineous couples within the RCC area, Bangladesh

Congenital malformations (CMF)	No. children from 70 CM			No. children from 100 NCM		
	Males	Females	Total	Males	Females	Total
Blind (BL)	1	2	3	0	0	0
Cerebral palsy (CP)	3	13	16	0	0	0
Crossed-eyes (CE)	1	3	4	0	1	1
Deaf-mute (DM)	1	1	2	0	0	0
Down's syndrome (DS)	0	1	1	0	0	0
Mental retardation (MR)	11	26	37	0	0	0
Microcephaly (MC)	3	0	3	0	0	0
Polydactyly (PD)	0	0	0	1	0	1
Syndactyly (SD)	1	0	1	0	0	0
Total affected	21	46	67	1	1	2
Normal	73	65	138	137	128	265
Grand total	94	111	205	138	129	267
Frequencies of CMF	(67×100÷205)= 32.68			(2×100÷267)= 0.75		

CM= consanguineous marriages; NCM= non-consanguineous marriages.

Plate 1 Deaf-mute

Plate 2 Cerebral palsy

Plate 3 Mentally retarded

Plate 4 Blind

Plate 5 Syndactyly

Plate 6 Mentally retarded and blind

Plates 1-6. Various congenital malformations (CMF) in children from consanguineous marriages (CM) within the RCC area, Bangladesh

Ben Arab *et al.* (1990) reported hearing impairment and deafness in children from consanguineous marriages. In addition, hearing loss, blindness, congenital glaucoma, cerebral lipidoses and mental retardation associated with decreased IQ scores and increased levels of intellectual disabilities are common in the first cousin marriages compared to the non-consanguineous unions (Bittles, 2003; Bittles *et al*., 2002). According to a later investigation, deafness and retinal dystrophies leading to blindness are prevalent in the children from the first cousin marriages in North Africa, the Middle East and large parts of Asia due to the expression of detrimental recessive genes (Saggara & Bittles, 2008).

As regards the incidences of various congenital defects in children from CM, Al-Hakeem & Hamamy (1992) found substantially high proportions of recessively inherited mental and physical handicapped children in Iraq. Childhood blindness was found to be associated with consanguinity in the West Bank and Gaza Strip population (Elder & De Cock, 1993). Al-Abdulkareem & Ballal (1998) reported 80% single-gene autosomal recessive disorders and 22% CMF in 16,419 babies from CM in the urban areas of Saudi Arabia. Modell & Darr (2002) noticed increased birth prevalence of infants with severe recessive disorders in CM. While syndactyly or webbed fingers is reported to be the most common CMF of the limbs and the condition occurs about 1 in every 2000-3000 live births, it is twice as common in males, and is 10 times more common in whites than blacks (Flatt, 2005; Mandal *et al.*, 2008). These findings are in well agreement with the present results.

Bener *et al.* (2007) showed higher rates of mental disorders and hearing deficit in children from first-cousins in the urban and semi-urban areas of Qatar. An appreciably high proportion of children (4.1%) from first-cousin marriages in Jordan suffered from congenital anomalies (Obeidat *et al*., 2008). The present results conform to the above findings in that relatively high numbers of the mental retardation (n=37), cerebral palsy (n=16), crossed-eyes (n=4), blindness (n=3) and microcephaly (n=3) appeared in offspring from consanguineous couples in the RCC area. Considering relatively a small sample size (n= 205 children from 70 CM), the frequencies of CMF in urban Rajshahi appeared to be too high.

In Morocco, Jaouad *et al*. (2009) demonstrated 176 families with autosomal recessive disorders where CM comprised 59.09% of all marriages. An earlier study by Islam & Ahmed (2009) in Rajshahi, Bangladesh revealed association between consanguinity and various birth defects and CMF that explained demerits of the prevailing tradition of marrying close relatives in our societies. Significant differences in the occurrence of genetic diseases in offspring from CM (4.88%) compared to those of NCM (4.13%) in

Kuwait was reported by Al-Kandari & Crews (2011), while Chinthapalli (2013) followed 13776 pregnancies in Bradford, UK, and found that 6.1% of children born to first cousins had congenital anomalies and that 98% of these children were born to people of Pakistani origin. The first cousin marriages were the most common type of CM among Arabs in Israel but the rates were found to decrease from 2000 to 2009 (Na'amnih *et al*., 2015). In contrast, first cousin marriages are still rather common nowadays around the world and in fact, in certain parts of Turkey, the percentage of CM has increased in recent years (Wong, 2015). Another study by Barrett (2016) revealed that the number of CM has grown in the subpopulations in the European countries like England and Ireland in the past decade, particularly among Pakistanis, Nigerians and Indians. According to a recent study, consanguinity is practiced by up to 10% of the world's population with rates ranging from 80.6% in certain provinces in the Middle East to less than 1% in western societies (Oniya *et al*., 2019). Apart from Islam & Ahmed (2009), however, there is no report available to compare the prevalence and/or incidence of CM in the urban or rural Bangladesh, the RCC in particular.

Recommendations: Keeping the aforesaid discussion in mind, the present study recommends the following to the prospective couples in the study area and elsewhere in the country: (1) The negative and harmful impacts of marriages between close relatives on various birth abnormalities (BA) and congenital malformations (CMF) in the immediate progenies may be avoided by providing genetic counselling for the prospective couples; (2) The health risks associated with consanguinity could be lessened by the development of genetic educational guidelines targeted to the public and the health sector professionals; and (3) By providing pre-implantation genetic diagnosis and pregnancy screening available at low costs, it might be possible to mitigate some of the harmful reproductive consequences associated with consanguinity.

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REFERENCES

Al-Abdulkareem, A. A. and Ballal, S. G. 1998. Consanguineous marriage in an urban area of Saudi Arabia: rates and adverse health effects on the offspring. *J. Com. Health* **23:** 75-83.

Al-Hakeem, S. and Hamamy, H. 1992. Genetic studies on institutionalized mentally retarded males with special reference to fragile X syndrome. Unpubl. MSc Thesis, Al-Mustansiriyah Medical College, Bagdad, Iraq.

Al-Kandari, Y. Y. and Crews, D. E. 2011. The effect of consanguinity on congenital disabilities in the Kuwaiti population. *J. Biosoc. Sci*. 43(1): 65-73.

Badaruddoza, M. A. and Akhtaruzzaman, M. 2007. Inbreeding and congenital heart diseases in a north Indian population. *Croat. Med. J*. **48(5):** 701-707.

Barrett, P. 2016. A review of consanguinity in Ireland--estimation of frequency and approaches to mitigate risks. *Ir. J. Med. Sci*. **185**(1): 17-28.

Ben Arab, S., Bonaiti-Pellie, C. and Belkahia, A. 1990. An epidemiological and genetic study of congenital profound deafness in Tunisia (Governorate of Nabeul). *J. Med. Genet.* **27(1):** 29-33.

Bener, A., Hussain, R. and Teebi, A. S. 2007. Consanguineous marriages and their effects on common adult diseases: Studies from an endogamous population. *Med. Princ. Pract.* **16:** 262-267.

Bittles, A. 2001. Consanguinity and its relevance to clinical genetics. *Clin. Genet*. **60**: 89-98.

Bittles, A. H. and Neel, J. V. 1994. The costs of human inbreeding and their implications for variations at the DNA level. *Nature Genet*. **8:** 117-121.

Bittles, A. H. 2002. The impact of consanguinity on the Indian population. *Indian J. Human Genet.* **8:** 45-51.

Bittles, A. H. 2003. Consanguineous marriage and childhood health. *Dev. Med. Child Neurol.* **45(8):** 571-576.

Bittles, A. H., Grant, J. C., Sullivan, S. G. and Hussain, R. 2002. Does inbreeding lead to decreased human fertility? *Ann. Hum. Biol*. **29:** 111-130.

Bittles, A. H., Mason, W. M., Greene, J. and Appaji, R. N. 1991. Reproductive behavior and health in consanguineous marriages. *Science* **252:** 789-794.

Bittles, A.H. 2013. Consanguineous marriages and congenital anomalies. *Lancet* 382(9901): 1316-1317.

Chinthapalli, K. 2013. First cousin marriage can double risk of birth defects. *British Med. J.* 347:f4374. doi: https://doi.org/10.1136/bmj.f4374.

Elder, M. J. and De Cock, R. 1993. Childhood blindness in the West Bank and Gaza Strip: Prevalence, etiology and hereditary factors. *Eye* **7:** 580-583.

Emery, A. E. H. and Mueller, R. F. 1992. *Elements of Medical Genetics* (8th edn.). Longman Group UK Ltd. pp. 349.

Flatt, A. E. 2005. Webbed fingers. *Proc. Bayl. Univ. Med. Cent.* **18(1):** 26-37.

Ghina, M., Hala, T., Mona, K., Marwan, K., Mustafa, K., Gerard, W. and Yunis, K. A. 2007. Effect of consanguinity on birth weight for gestational age in a developing country. *Am. J. Epidemiol.* **165(7):** 742-752.

Hamamy, H. 2012. Consanguineous marriages: Preconception consultation in primary health care settings. *J. Community Genet*. **3**: 185-192.

Hussain, R., Bittles, A. H. and Sullivan, S. 2001. Consanguinity and early mortality in the Muslim populations of India and Pakistan. *Am. J. Hum. Biol*. **13:** 777-787.

Islam, M. S. and Ahmed, S. 2009. Incidences of birth abnormalities and congenital defects and their association with consanguineous marriages in Rajshahi: A case study. *J. bio-sci*. **17:** 107-112.

Jaouad, I.C., Elalaoui, S. C., Sbiti, A., Elkerh, F., Belmahi, L. and Sefiani, A. 2009. Consanguineous marriages in Morocco and the consequence for the incidence of autosomal recessive disorders. *J. Biosoc. Sci.* **41**(5): 575-581.

Kerkeni, E., Monastiri, K., Seket, B., Guediche, M. N. and Cheikh, H. B. 2007. Interplay of socio-economic factors, consanguinity, fertility, and offspring mortality in Monastir, Tunisia. *Croat. Med. J*. **48(5):** 710–717.

Mandal, K., Phadke, S. R. and Kalita, J. 2008. Congenital swan neck deformity of fingers with syndactyly. *Clin. Dysmorphol.* **17(2):** 109-111.

Modell, B. and Darr, A. 2002. Genetic counselling and customary consanguineous marriage. *Nature Reviews Genetics* **3**: 225-229.

Morton, N. E. 1958. Empirical risks in consanguineous marriages: Birth weight, gestation time and measurement of infants. *Am. J. Hum. Genet*. **1:** 344-349.

Morton, N. E. 1961. Morbidity of children from consanguineous marriages. *Prog. Med. Genet*. **1:** 261-291.

Na'amnih, W., Romano-Zelekha, O., Kabaha, A., Rubin, L. P., Bilenko, N., Jaber, L., Honovich, M. and Shohat, T. 2015. Continuous decrease of consanguineous marriages among Arabs in Israel. *Am. J. Hum. Biol*. **27**(1): 94-98.

Ng, D. 2016. The implications of parental consanguinity on the care of neonates. *Adv. Neonatal Care* 16(4): 273-282.

Nouri, N., Nouri, N., Tirgar, S., Soleimani, E., Yazdani, V., Zahedi, F., and Larijani, B. 2017. Consanguineous marriages in the genetic counselling centers of Isfahan and the ethical issues of clinical consultations. *J. Med. Ethics Hist. Med*. **10**: 12.

Novitski, E. (1977) *Human Genetics.* Mcmillan Publ. Co. Inc., New York, USA. pp. 458.

Obeidat, B. R., Khader, Y. S., Amarin, Z. O., Kassawneh, M. and Omari, M. A. 2008. Consanguinity and adverse pregnancy outcomes: The North of Jordan experience. *Mat. Child Health J*. **14:** 232-240.

Oniya, O., Neves, K., Ahmed, B. and Konje, J. C. 2019. A review of the reproductive consequences of consanguinity. *Eur. J. Obstet. Gynecol. Reprod. Biol*. **232**: 87-96.

Saggara, R. A. and Bittles, A H. 2008. Consanguinity and child health. *Paed. Child Health* **18(5):** 244-249.

Shawky, R. M., Elsayed, S. M., Zaki, M. E., El-Din, S. M. N. and Kamal, F. M. 2013. Consanguinity and its relevance to clinical genetics. *Egyptian J. Med. Hum. Genet*. **14**: 157-164.

Søgaard, M, and Vedsted-Jakobsen, A. 2003. Consanguinity and congenital abnormalities (article in Danish). *Ugeskr Laeger* **165**(18): 1851-1855.

Tayebi, N, Yazdani, K. and Naghshi, N. 2010. The prevalence of congenital malformations and its correlation with consanguineous marriages. *Oman Med. J*. **25**(1): 37-40.

Teeuw, M. E., Loukili, G., Bartels, E. A. C., ten Kate, L. P. Cornel, M. C. and Henneman, L. 2014. Consanguineous marriage and reproductive risk: attitudes and understanding of ethnic groups practicing consanguinity in Western society. *Eur. J. Hum. Genet*. **22**: 452-457.

Wong, K. V. 2015. Cousin marriages from viewpoint of Genetics. Doi: 10.14205/2311-0309.2014.02.02.4. Available at https://www.researchgate.net/publication/273295363.