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ORIGINAL ARTICLE

Demographic and biochemical parameters in Pakistani families having child with spina bifida.

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ABSTRACT… Objective: To find out the association of demographic and biochemical markers in families of the patients with spinabifida. **Study Design:** Cross Sectional study. **Setting:** Arif Memorial Teaching Hospital, Lahore, Sheikh Zayed Hospital, Lahore, Hameed Latif Hospital Lahore. **Period:** July 2017 to January 2018. **Material & Methods:** Demographic data of the participants was obtained through a pre designed questionnaire with informed consent. Physical examination of weight and height for the calculation of BMI was done at spot. Biochemical markers such as HbA1c and folic acid were measured after collecting 5ml blood samples of participants through automated analyzers. **Results:** Results of this study showed 50% mothers bearing child with spina bifida being between the ages of 26 to 30 years. 50% of Fathers of subjects were between 35 to 40 years of age. 62.5% subject families belonged to rural area. 87.5% families having child with spina bifida belonged to low SES (Socioeconomic Statius). 50% Consanguinity found in subject families. BMI, HbA1c and folic acid of children were found to be significant p values respectively 0.046, 0.043 and 0.005. BMI of fathers also showed significant p value of 0.043. **Conclusion:** Demographic data such as age, location and socioeconomic status of parents of subjects were found to be significantly correlated with the occurrence of spina bifida, while BMI of fathers subjects were found having effect on the spina bifida in their children.

Key words: Folic Acid, Hba1c, Spinabifida, SES.

INTRODUCTION

Congenital defects are the leading cause of death in developed countries and the second most common cause of death in many developing countries. These defects occur very early, usually during the first month of embryonic development, when even the diagnosis of pregnancy may be uncertain.[1]

Spina bifida is one of the most common presentations of neural tube defects, affecting 1 of 2,500 newborns worldwide. Prevalence and incidence of Spina Bifida varies by geographic region and ethnicity, due to unknown reasons. The highest incidence rates are observed in countries such as the United Kingdom, Ireland and Pakistan, the lowest in Finland, Japan and Israel.[2]

The neural tube closes between the 18 to 28 days of intrauterine life, along 5 distinct sites.[3] NTD is causes un closure of any of these site. The damage to the spinal cord is due to the destruction of the caudal nerve pore, which occurs no later than the 26th day. The least serious is Spina bifida occulta, in which the skin and vertebrae are abnormal but do not involve the spinal cord. In the mylomeningocele, the most serious type of spina bifida, the nervous tissue covered by the meninges protrudes through the vertebral column. This condition may be related to different degrees of paralysis caused by spinal cord injury in children.[4]

Genetic and environmental factors are thought to be contributing to the etiology of NTDs.[5] Known risk factors for neural tube defect are births with

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previous NTD, family history of NTDs, patients with low socio-economic status, obesity, folic acid deficiency , hyperthermia in early pregnancy and known history of diabetes or epilepsy in the mother.[6]

The geographical differences observed for the NTDs between countries and sometimes within countries are still reported. For a long time, it was assumed that socio-economic conditions might cause neural tube defects, and that the incidence of spina bifida in lower socio-economic status groups was generally higher. Even after adjusting for the use of multivitamins, this association still exists.[4]

It has long been reported that children born to women with lower socioeconomic status are more likely to experience neural tube defects. However, few studies have explored these findings to find further clues about the cause of neural tube defects. It is still unclear whether the increased risk is solely the result of known risk factors, such as fewer intakes of multivitamins by mothers. The study found that lower hospitalization rates for lower SES increased the risk of neural tube defects during pregnancy, with adjusted odds ranging from 1.5 to 2.4. In addition, under the gradient of the lower socioeconomic status indicator, the risk appears to increase.[7]

The literature on the possible link between maternal age and neural tube defects is considered very confusing. The most commonly reported variants showed a U-shaped relationship between the prevalence of neural tube defects and maternal age, a higher ratio of mothers under 20 years of age, and over 35, between 20 to 24 or 25 and 29 years.[1]

Consanguineous marriages are a favored feature in Pakistan, social, cultural, ethnic and economic reasons. Approximately 30% cases may have mental retardation, congenital anomalies and dysmorphisms and these disorders are autosomal recessive disorders are linked with consanguinity.[8]

Moore LL conducted research in 2000 on meternal obesity and diabetes are associated with the development of congenital malformations. Some studies have shown that maternal obesity is associated with an increased risk of abnormal neural tube outcomes, including spina bifida, although not all studies are consistent.[9] Abnormally high levels of glucose in the mother's blood cause an increase in glucose transport to the embryo, which is responsible for the teratogenicity. Even so, even in the 21st century, congenital diabetes-related abnormalities, particularly congenital defects affecting the neural tube and heart, have been reported with a significant increase (up to 5-fold).[10]

The cause of NTDs is multifactorial and folic acid is the main known factor. Folic acid deficiency affects the development of the skull and spinal cord. Insufficient folate intake or defective absorption of folate can cause neural tube problems.[4]

This study is the first of its kind in our country which aims at documenting the relationship of various biochemical markers and demographic variables in the families having child with spina bifida.

MATERIAL & METHODS

A cross sectional survey was conducted in Arif memorial teaching hospital, Lahore, Sheikh Zayed hospital, Lahore, Hameed Latif hospital, Lahore to find out the relationship of biochemical and demographic factors with spina bifida. Duration of the study was July 2017 to January2018. The study protocol was approved by university of Lahore (IMBB/UOL/19/323). Sample size was calculated using prevalence of spina bifida in Pakistani population through OpenEpi online calculator by using 95% confidence level and 5% confidence interval.

After taking informed consent, researcher has taken 40 families in which 24 families were appointed as subject, having a child with spina bifida while the other 16 families were appointed as control, having normal child. The families participated in the study consisted of a child, father and mother, while other members of family

were excluded. Subject selection criterion was that, the patient was having any form of Spina Bifida, while controls were the normal children having no congenital anomaly. Demographic data was collected through a questionnaire developed by literature review and expert opinion, which comprised age, settlement, occupation, and consanguinity. BMI was calculated with the help of physical examination of height and weight. While HbA1c and Folic acid levels were tested through blood. 5ml of the whole blood was collected from cubital vein of subjects and controls, using BD syringe Becton Dickinson (pvt) Ltd, Lahore, *Pakistan* then 3ml for HbA1c transferred in K3-EDTA coated sterile vacationers while 2ml was transferred to serum gel separator tube for folic acid test. Whole blood was collected in a serum separator tube and allowed to stand at room temperature for 30 minutes before being centrifuged at 1500 rpm for 15 minutes and then pipetted out serum and transferred to separate sterile vial and the samples were immediately transferred to icebox and later stored at 4°C till further processing. Descriptive analysis of the demographic information frequency and percentage was calculated and for inferential statistics, independent sample t-test was applied.

RESULTS

The demographic characteristics of the study of the participants reflected the population characteristics of Pakistan. Most of the cases and controls participants were from low socioeconomic status, relatively young and belonged to rural areas, and all women were house wives.

Above table showed that most of children are in 0 to 5 years of age, subjects 24(100%) and controls 8(50%). Similarly most of mothers bearing child with spina bifida are between the ages of 26 to 30 years. Majority of Fathers, subjects and controls are between 31 to 34 years of age. Most of the participants are from rural area and belong to low socioeconomic class.

Variable	Ranges	Subjects	Controls
Age(years) Children	0 to 5	24(100%)	8 (50%)
	6 to 10	0	8 (50%)
Mothers	21-25	0	4(25%)
	26-30	12(50%)	6(37.5%)
	31-35	9(37.5%)	4(25%)
	36-40	3(12.5%)	2(12,5%)
Fathers	26-30	0	2(12,5%)
	31-35	9(37.5%)	4(25%)
	36-40	12(50%)	8(50%)
	41-45	3(12.5%)	2(12,5%)
Settlement	Urban	9(37.5%)	8(50%)
	Rural	15(62.5%)	8(50%)
Occupation	Labor	21(87.5%)	8(50%)
	Employee	3(12,5%)	4(25%)
	Business	0	4(25%)
Consanguinity	Yes	12(50%)	4(25%)
	No	12(50%)	12(75%)

Table-I. Demographic data of the participants.

Family Members	Participants	N 120	Descriptive Analysis	BMI	HbA1c	Folic Acid
Children	Subject	24	Mean±SD	17.975±2.173	4.637±0.542	12.075± 1.019
	Control	16	Mean±SD	15.975±1.291	5.425±0.820	15.337±2.308
			P value	0.042	0.003	0.040
Fathers	Subject	24	Mean±SD	25.625±0.969	15.487±2.402	5.312±0.581
	Control	16	Mean±SD	22.550±3.498	15.112±1.410	5.812±0.513
			P value	0.031	0.709	0.090
Mothers	Subject	24	Mean±SD	25.050±1.905	16.125±1.627	5.587±1.372
	Control	16	Mean±SD	24.900±3.489	16.231±2.150	5.462±0.870
			P value	0.917	0.913	0.831

Table-II. Mean and standard deviation of biochemical parameters.

BMI, folic acid and HbA1c show the significant results in children because the P-value≤0.05. In fathers BMI showed the significant value 0.031. No significant result found in Mothers BMI, folic acid and HbA1c.

DISCUSSION

In the present study 50% of the subject fathers fall in the range of 36 to 40 years. The results of present research identical to another research findings published in 2010, The results of this research concluded that paternal age is the one of common risk factor of some multifactorial birth defects.[11,12,13] However one study by Shaw in 1994 were showing the results in contrast of above relations that paternal age is not related to NTDs.[14]

Results of this study showed positive relation of spina bifida with the age of mother. Most of the subject mothers are falling in range of 26 to 30 years 50% and between 31 to 35 years 37.5% of the age. An increased maternal age from 20-29 years causes increase risk of baby with Spina Bifida.[15] In contrast, other, study found no relationship between NTDs and maternal age.[16]

The present study revealed that most of the families are bearing child with spina bifida belonging to rural areas 62.5%. In a research conducted in India supported the similar results.[17] The data showed that the incidence of NTDs was 6·57–8·21 per 1000 live births in least developed areas of India, which is among the highest worldwide.[18]

The study showed that majority of subject families belonging to low SES 87.5%. It has been observed that Low socioeconomic class parents having greater risk of offspring with NTD in several countries including Europe, North America.[19] A study conducted in Los Angeles showing no association between socioeconomic class and risk for NTD.[15]

Consanguineous Marriages within the family is still more common in south Asia particularly in Pakistan.[20] Regarding cousin marriages, in this study 50% subject couples are consanguineous. While in another study conducted on neural tube defects 60% case couples were consanguineous.[8,21,22] Palestinian population have higher incidence of malformations among children coming from consanguineous marriages.[23]

In the present study mean value of BMI in the subject children 17.97 that is significantly different from the mean value 15.97 of BMI in controls children. This result is supported by another study conducted by Van who described that children with myelomeningocele had higher body fat (35.2% versus 29.9%, p=0.01).[24] Obesity can impose significant personal and economic hardship on the child and family.[25,26] But in contrast to the other studies Dosa NP said that obesity in general population and child with Spina Bifida is same.[27]

This study found significant difference from t-test values among the paternal BMI values that is 0.031 in difference among the subject and controls mothers BMI from t- test which is 0.917. Other systematic reviews have demonstrated that as the severity of maternal obesity increased, the risk for NTDs increased too.[29] The relation between maternal BMI and NTDs showed an increasing risk especially for spina bifida, with increasing BMI.[30,31]

HbA1C showed significant difference among subject and control children that is 0.043. But HbA1C in subject and controls parents show non-significant difference that is 0.090 in fathers and 0.917 in mothers. Diabetic mother having two time more tendency having child with spina bifada as compared to non-diabetic mother, Mills et al found.[32,33]

Folic acid t-test value showed significant difference in subject and control children that is 0.005.This result contradicts the study conducted by Korzeniecka in 2014 who described serum FA level was in normal range in MMC patients.[34] While in subject and controls fathers the level of folic acid show non-significant difference that is 0.710 for fathers and 0.913 for mothers. One study conducted in Bangladesh to find the

protective effects of folic acid, results of this study confirms the protective association between maternal prenatal folic acid supplement use and myelomeningocele among children born.[35,36]

CONCLUSION

This study concludes that maternal biochemical marker HbA1c, BMI and folic acid showed significant association with spina bifida in children and also in the BMI of fathers.

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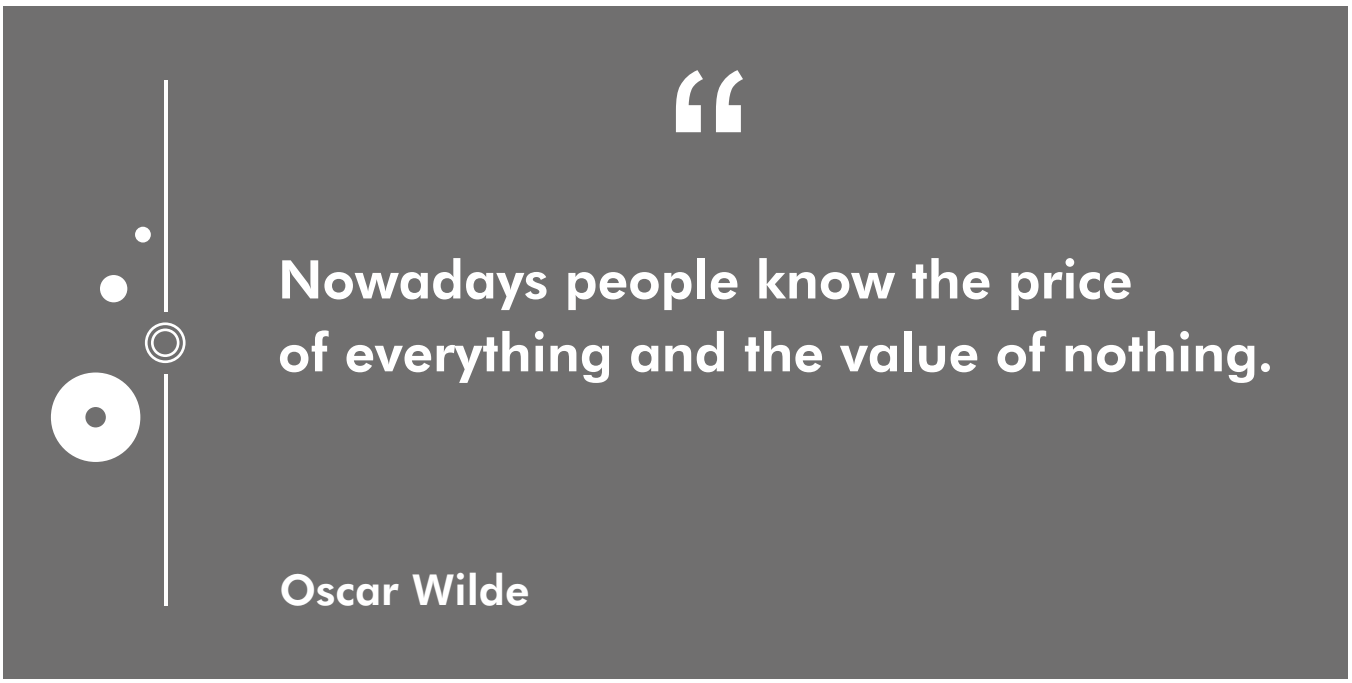

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3	Arif Malik	Review.	
4	Gull-e-Faran	Final review.	
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