American Journal of Pediatrics
2023; 9(3): 164-170
http://www.sciencepublishinggroup.com/j/ajp
doi: 10.11648/j.ajp.20230903.20
ISSN: 2472-0887 (Print); ISSN: 2472-0909 (Online)

Effect of Periconceptional Life Style Factors on Occurrence of Birth Defect

Nusrat Shams[1, *], Monir Hossain[2], Mahfuza Shirin[2], Husnea Ara Khan[1], Mohammad Mohsin[3]

[1]Department of Paediatrics, National Institute of Neurosciences and Hospital, Dhaka, Bangladesh

[2]Department of Critical Care Paediatrics, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh

[3]Department of Paediatrics, Kuwait Bangladesh Friendship Government Hospital, Dhaka, Bangladesh

Email address:

nusratshams99@gmail.com (Nusrat Shams)

[*]Corresponding author

To cite this article:

Nusrat Shams, Monir Hossain, Mahfuza Shirin, Husnea Ara Khan, Mohammad Mohsin. Effect of Periconceptional Life Style Factors on Occurrence of Birth Defect. *American Journal of Pediatrics*. Vol. 9, No. 3, 2023, pp. 164-170. doi: 10.11648/j.ajp.20230903.20

Received: June 10, 2023; **Accepted**: July 4, 2023; **Published**: August 22, 2023

Abstract: Globally, birth defects (BDs) affect approximately 3-5% of infants and can arise during intrauterine life, remaining present at birth regardless of whether they are immediately recognized. These defects can be caused by a variety of factors, including chromosomal anomalies, multifactorial etiology, single gene disorders, and environmental influences; however, the cause remains unknown in many cases. Among the various causes, periconceptional factors play a crucial role in influencing the critical period of organogenesis. Therefore, the aim of this case-control study conducted at the Pediatric Surgery and Medicine Department in Dhaka Shishu (Children) Hospital, Bangladesh, from January 2012 to December 2013 was to assess the impact of periconceptional lifestyle factors on the occurrence of birth defects. The study included 280 infants aged 0-364 days, with an equal number of cases presenting structural birth defects and controls without any birth defects. Detailed examinations and relevant investigations were conducted for each subject, and data analysis was performed using SPSS 16.0 version through univariate, bivariate, and multivariate analyses, with results presented in tables and graphs. The study revealed significant associations between birth defects and several lifestyle factors, including advanced parental age (>30 years), parental illiteracy, maternal low BMI, low socio-economic condition, rural residency, paternal insecticide exposure, prolonged sunlight exposure, parental tobacco exposure in various forms, use of coal stove for cooking, and inadequate dietary intake of meat, fish, milk, egg, and pulses. These findings emphasize the importance of preventive measures through pre-conceptional and periconceptional care to modify these lifestyle factors and reduce the incidence of birth defects.

Keywords: Periconceptional Lifestyle, Birth-Defect, Anomaly, Causative Factors

1. Introduction

Birth defect (BD) is a term used to describe structural, functional and metabolic disorders present at birth and it is synonymous with congenital anomaly [1]. According to the World Health Organization (WHO) [2], the term 'congenital malformations' should be confined to structural defects at birth [3]. Birth defects can be isolated abnormalities or part of a syndrome and continue to be an important cause of neonatal and infant morbidity and mortality [4]. Birth defects or congenital anomalies are relatively common. It is estimated that, 1 in 40 or 2.5 % of newborns, have a recognizable malformation or malformations at birth [4] affecting 3% to 5% of live births in the United States [1] and 2.1% in Europe [5]. In India, congenital anomalies account for 8% to 15% of perinatal deaths [6] and 13% to 16% of neonatal deaths [7, 8]. In Bangladesh, hospital-based prevalence showed 2-4% of birth defects in different studies [9-13]. Among causes periconceptional lifestyle is an important issue as it reflects exposure to various potential teratogens. Periconceptional lifestyle can be defined as lifestyle activities, i.e., habit, economic level, education, diet, level of physical activities, substance abuse, social and personal interactions and occupational as well as environmental exposures, relating to, or done during the period from before conception to the third month of pregnancy [14-16]. A commonly held but erroneous view is that, birth defects are not a public health issue in developing countries [17]. According to WHO's (2013) [18] report on IMR in SEARA, the country has a rate of 37/1000 live births, with birth defects being the fifth most common cause of IMR (National Neonatal Health Strategy 2009). Another consequence of birth defects is the risk of having more severe clinical complications, a higher number of hospitalizations and also unbearable social and mental costs. Indicating those, it is the right time to understand the real situation and to take the preventive measures. But preventive measures can be taken only when causes are identified. With this view, this study was conducted to identify the effect of periconceptional lifestyle factors on the occurrence of birth defects.

2. Materials & Methods

This case-control study was conducted at both the Pediatric Surgery and Medicine Department in Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh during the period from January 2012 to December 2013. In total 280 infants of 0-364 days old were included as the study subjects. In subject selection, non-probability convenient and purposive sampling technic was used. All subjects were divided into two groups; cases having the structural birth defect and controls without any birth defect. Cases and controls were equal in number. A predesigned questionnaire was introduced after getting informed written consent from the mothers. Each infant included was exposed to full examination to identify the defect and relevant investigations as per unit protocol were done. A meticulous examination of each baby was done to find out the anomaly as precisely as possible. Anthropometric measurements of mothers to calculate the maternal BMI was made. With the permission of mothers, photographs of all the cases were taken. The whole study was conducted in accordance with the principles of human research specified in the Helsinki Declaration and executed in compliance with currently applicable regulations and the provisions of the General Data Protection Regulation (GDPR). All the demographic and clinical data of the participants were recorded. A predesigned questioner was used in data collection. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 16.0 program as per necessity.

3. Results

In this study, birth defects were found more commonly in elderly mothers and older fathers. Birth defects were also more common in low maternal BMI and low monthly income groups. The mean ±SD age of the babies was 87.17±10.56 days in case group and in the control group, it was found as 67.50±92.42 days. Among the participants, 44 (31.4%) mothers of the case and 18 (12.9%) mothers of the control group was illiterate. Birth defects were significantly higher in illiterate mothers, $p<0.05$. OR [95%CI] for illiterate mother, was 3.11 [1.69-5.71]. Among the participants, 39 (27.9%) fathers of the case and 21 (15%) fathers of the control group was illiterate. Birth defects were significantly higher in illiterate fathers, $p<0.05$. OR [95% CI] for illiterate father was 2.19 [1.21-3.97]. Among total cases, working mother was higher among case group 5 (3.6%) versus 2 (1.4) in the control group and it was a risk factor for BD, 2.55 [95% Cl: 0.487-13.39] though the result was not statistically significant. Rural residence was significantly (p 0.05) higher among cases 111 (79.3%) than in the control group 77 (55%); OR [95% CI] for rural residences was 3.13 [1.85-5.31]. NVD was found in higher frequency in control group (80%) than that in cases group (64.3%). On the other hand, LUCS was found in higher frequency in case group (37.7%) than that in control group (20%). The differences were statistically significant ($p<0.05$) between the groups. Among all participants, paternal insecticide exposure was present in 39 (27.9%) fathers of the case group and 15 (10.7%) fathers of the control group; the difference was statistically significant ($p<0.05$). Paternal fertilizer exposure was present in 40 (28.6%) fathers of the case group and 14 (10%) fathers of the control group, the difference was statistically significant ($p<0.05$). Prolonged sunlight exposure was present in 50 (35.7%) fathers of the case group and 26 (18.6%) fathers of the control group, the difference was statistically significant t ($p<0.05$). Smoking habit was present in 91 (65%) fathers of the case group; the difference was statistically significant ($p<0.05$). Among the participants, passive smoking was present in 30 (21.4%) mothers of the case group and 9 (6.4%) mothers of the control group; the difference was statistically significant ($p<0.05$). A habit of smokeless tobacco taking was present in 15 (10.8%) mothers of the case group and 3 (2.1%) mothers of the control group; the difference was statistically significant ($p<0.05$). Cooking in a kitchen was present in 129 (92.1%) mothers of the case group and 117 (87.9) mothers of the control group; the difference was statistically significant ($p<0.05$). Coal stove for cooking was used by 103 (73.6%) mothers of the case group and 60 (42.9%) mothers of the control group; the difference was statistically significant ($p<0.05$). Among total cases, consanguinity among parents was found in 22 (15.7%) cases and 17 (12.1%) in controls. The difference was not statistically significant ($p>0.05$); OR [95% CI] for consanguinity was 1.35 [0.68-2.67]. In this study, history of HTN was present in 6 (4.3%) mothers belonging to the case group and 3 (2.1%) mothers of the control group; the difference was not statistically significant ($p>0.05$) and OR was 2.05 [0.50-8.34] for HTN. History of DM was present in 5 (3.6%) mothers belonging to the case group and 1 (0.7%) mothers of the control group; the difference was not statistically significant ($p>0.05$) and OR was 2.04 [1.81-2.30] for DM. Among the participants, mothers who took fish once or less than once a week experienced BD more and the difference was statistically significant ($p< 0.05$) between the groups. Mothers who eat meat, fish, egg or dairy products ≤ once/week experienced BD significantly. Among all of our cases, most of the defects were distributed to the gastrointestinal system (18%), Genito urinary system (16%), CVS (14%), NTD (13%), defect of the face (13%) and skull (11%). In addition, limb defects (5%), others defects (eye, ear, skin, and chest) in 4%, abdominal defects in 3%, and syndromic defects in 3% of patients. Among the cases, isolated defect was in 80% of patients, multiple defects in 17% of patient and 3% syndromes were present. No response from the mothers regarding smoking, alcohol, tea, and coffee consumption was found, so those factors were not analyzed. In this study, analysis in the regression model showed significant risk factors were: maternal age >30 years, paternal smoking, maternal DM, maternal passive smoking, use of coal stove for cooking and less consumption of meat, fish, milk, and vegetables. Intake of folic acid and multivitamins before 2 months of pregnancy were significantly protective against any form of birth defect.

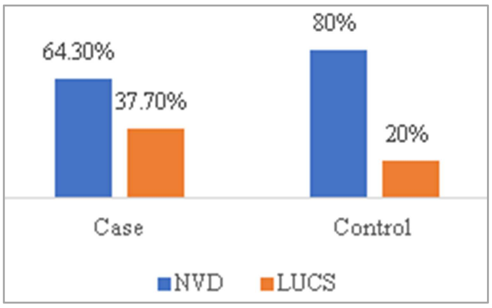

Figure 1. *Distribution of the respondents by mode of delivery.*

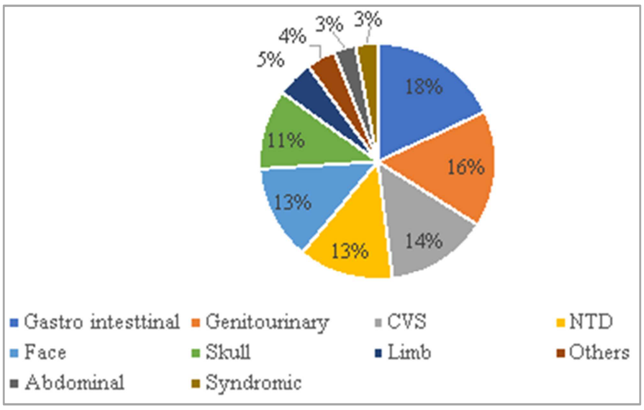

Figure 2. *Distribution of the birth defects according to the system.*

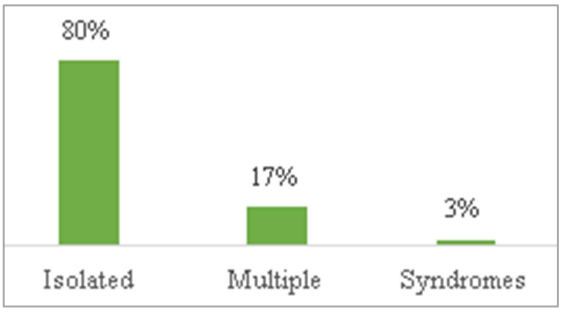

Figure 3. *Distribution of birth defects by the number of organs involved.*

Table 1. *Distribution of respondents by demographic characteristics (N=280).*

Variables	Cases (n=140) Mean ± SD	Controls (n=140) Mean ± SD	P Value
Age of the patient (Days)	87.17±10.56	67.50±92.42	0.102
Maternal age (Years)	25.86±5.20	23.41±4.65	0.0001
Paternal age (Years)	32.10±5.39	29.85±6.38	0.002
Maternal BMI (Kg/m2)	22.7±3.003	23.35±2.54	0.0001

Table 2. *Distribution of respondents by maternal education (N=280).*

Maternal Education	Case (%)	Control (%)	OR [95% CI]	P Value
Illiterate	44 (31.4)	18 (12.9)		
Educated	96 (68.6)	122 (12.9)	3.11 [1.69-5.71]	0.0001
Total	140	140		

Table 3. *Distribution of respondents by paternal education (N=280).*

Paternal Education	Case (%)	Control (%)	OR [95% CI]	P Value
Illiterate	39 (27.9)	21 (15)		
Educated	101 (72.1)	119 (85)	2.19 [1.21-3.97]	0.01
Total	140	140		

Table 4. *Distribution of respondents by maternal occupation (N=280).*

Occupation of Mother	Case (%)	Control (%)	OR [95% CI]	P Value
Working mother	5 (3.6)	2 (1.4)		
Non-working mother	135 (96.4)	138 (98.6)	2.55 [0.49-13.39]	0.45
Total	140	140		

Table 5. *Distribution of respondents by residence (N=280).*

Residence	Case (%)	Control (%)	OR [95% CI]	P Value
Rural Yes	111 (79.3)	77 (55)		
No	28 (20)	60 (42.9)	3.13 [1.85-5.31]	0.0001*
Base	139	137		

Table 6. *Distribution of respondents by paternal exposure (N=280).*

Paternal Exposure	Case %	Control %	P value
Insecticide's exposure	39 (27.9)	15 (10.7)	0.0001
Fertilizer exposure	40 (28.6)	14 (10.0)	0.0001
Prolonged sunlight exposure	50 (35.7)	26 (18.6)	0.001
Smoking	91 (65.0)	49 (35.0)	0.0001

Table 7. *Distribution of respondents by maternal uses (N=280).*

Maternal uses	Case (%)	Control (%)	P Value
Passive smoking	30 (21.4)	9 (6.4)	0.001
Maternal smokeless tobacco	15 (10.8)	3 (2.1)	0.003
Cooking in a kitchen	129 (92.1)	117 (83.6)	0.043
Use of coal stove	103 (73.6)	60 (42.9)	0.0001

Table 8. *Distribution of respondents by parental consanguinity (N=280).*

Consanguinity	Case (%)	Control (%)	OR [95% CI]	P Value
Present	22 (15.7)	17 (12.1)		
Absent	118 (84.3)	123 (87.9)	1.35 [0.68-2.67]	0.50
Total	140	140		

Table 9. *Distribution of respondents by maternal comorbidity (N=280).*

Co-morbidity	Case (%)	Control (%)	OR [95% CI]	P Value
HTN Yes	6 (4.3)	3 (2.1)		
No	134 (95.7)	137 (97.9)	2.04 [.50-8.34]	0.5
Total	140	140		
DM Yes	5 (3.6)	1 (0.7)		
No	135 (96.4)	139 (99.3)	2.04 [1.81-2.30]	0.06
Total (%)	140	140		

Table 10. *Distribution of respondents by weekly dietary consumption (N=280).*

Weekly consumption	Case %	Control %	P value
Fish ≤ once/week	87 (62.1)	17 (12.1)	0.0001
Meat ≤ once/week	123 (87.9)	61 (43.6)	0.0001
Egg ≤ once/week	85 (60.7)	32 (22.9)	0.0001
Milk ≤ once/week	58 (41.4)	3 (2.1)	0.0001
Vegetable ≤ once/week	2 (1.4)	0 (0)	0.50

Table 11. *Multivariate regression analysis of lifestyle factors.*

Variables in multivariate analysis	Std. Error	sig.	95% confidence interval for Exp (B)	
			Lower Bound	Upper Bound
Socio-demographic status				
Rural residency	0.542	0.214	0.678	5.671
Maternal age 25-30 years	0.664	0.441	0.454	6.136
Maternal age > 30 years	1.188	0.002	3.721	391.818*
Paternal age 31-35 Years	0.675	0.315	0.525	7.39
>35 years	0.967	0.135	0.035	1.571
Maternal illiteracy	0.647	0.782	0.337	4.247
Paternal illiteracy	0.61	0.611	0.222	2.424
Low-socioeconomic status	0.675	0.362	0.144	2.031
Risk factors				
Paternal consanguinity	0.574	0.456	0.494	4.69
Prolonged sunlight exposure of father	0.676	0.685	0.202	2.861
Maternal DM	0.962	0.035	1.159	50.288*
Maternal HTN	1.182	0.343	0.302	31.163
Paternal smoking	0.458	0.049	1.003	6.047*
Maternal passive smoking	0.702	0.043	1.293	14.594*
Cooking in kitchen	0.738	0.719	0.18	3.259
Coal stove/solid wood use for cooking	0.624	0.041	1.294	10.917*
Maternal dietary consumption				
Meat consumption <once/week	0.557	0.005	1.616	14.3418
Egg consumption <once/week	0.524	0.005	0.164	1.283
Milk consumption <once/week	0.817	0.001	6.846	168.074*
Pulse consumption <once/week	0.947	0.373	0.363	14.869

Variables in multivariate analysis	Std. Error	sig.	95% confidence interval for Exp (B)	
			Lower Bound	Upper Bound
Vegetable consumption <once/week	1.046	0.136	0.612	36.875
Folic acid used	0.428	0.577	0.549	2.937
Folic acid used before two months	1.23	0.147	0.015	1.872

Significant*

4. Discussion

The aim of the study was to evaluate the effect of periconceptional lifestyle factors on the occurrence of birth defects. Though a newborn brings in its wake untold happiness to those around, there are some unfortunate babies whose birth is clouded with sadness and worry for the parents because of the BDs in them which manifest either immediately after birth or after a while depending on nature of the anomaly. A pediatrician may face the problems of congenital malformations in day-to-day practice in the form of failure to thrive, mental retardation, dysmorphism and recurrent infections. To the best of our knowledge, this is the first study conducted in Bangladesh that aimed to assess the lifestyle factors for certain birth defects at a tertiary care center. In this study, BDs were significantly higher among the maternal age >30 years. Raza et al. (2012) found most mothers, in their study group, were over the age of 30 [19]. Whereas Zhang et al. found significantly higher BDs among the maternal age less than 25 [20]. Most of the mothers and fathers were educated up to the level of high school both in the case and control group in this study and education of any level was protective against BD. Illiteracy of both parents was significantly associated with BD. This finding was similar to other studies [19, 21]. Though obesity is a well-recognized problem in many developed countries due to adverse pregnancy outcomes including BD [22-24]. In our country most mothers are undernourished. The mean BMI of most of the mothers in the case group was significantly lower than the controls in this study. Low BMI was significantly associated with BD. Yazdi et al. and Waller et al. (2007) [23, 24] found a positive association between maternal obesity with spina bifida and heart defects, anorectal atresia, hypospadias, limb reduction defects, diaphragmatic hernia, and omphalocele and a strong inverse association with gastroschisis. No study showed a relationship between BD and low BMI. Probably this difference may be due to a lack of adequate nutrients required during the period of organogenesis. In some other studies, BDs were more prevalent in rural areas. [20, 25] Residing in rural areas was a significantly higher risk factor. Rural residents may have some toxic environmental exposures easily like fertilizers and insecticides, which might be associated with BD. [26, 27] Association of BD with rural residency should be explored in the future. History of HTN and DM were not significant risk factors for BD in this study. Several studies found an association of DM with BD [10, 28] but no relation was observed for BD with HTN. But multivariate analysis of the present study showed that DM was a significant risk factor for BD. In this study prolonged sunlight exposure was significantly associated with BD. Most of the mothers in our country are housewives, only 2.8% were working mothers in this study. Non-significant association with BD was found in the case of working mothers. This might be due to stressful events [29] or some unknown environmental exposures. Though several studies revealed the association between the BDs and smoking [20, 30, 31] no study was carried out in our country to see the relationship. In this study paternal smoking habit was significantly associated with BD. The combustion of coal and biomass indoors emits a substantial number of toxic pollutants, including particulate matter, polycyclic aromatic hydrocarbons, carbon monoxide, and sulfur dioxide. [32] In Bangladesh, about 92% of women in rural areas and 35% of women in urban area use solid fuel for cooking. [33] Rahman and Azad (2009) [34] concluded with the findings that the use of solid fuels for cooking remained the biggest predictor of low maternal BMI. Low BMI is associated with low nutrition and may also cause BD. Moreover, temperature and gaseous fumes generated by stoves may cause some malformation. [35, 36] We have tried to explore maternal dietary habits in detail. Mothers who took fish, meat, egg, and milk less than once a week were significantly associated with BD. To the best of our knowledge, no study was conducted in our country to explore the detailed dietary habit of the mother. The intriguing findings of our study warrant further research. More powerful study designs are necessary to confirm the association between parental periconceptional lifestyle factors and birth defects.

5. Limitations of the Study

This was a hospital-based study. So, the findings of this study may not be a reflection of the general population of the whole country.

6. Conclusion

In conclusion, this study aimed to evaluate the impact of periconceptional lifestyle factors on the occurrence of birth defects (BDs). BDs can bring sadness and worry to parents, as they can lead to various challenges for the affected infants. The results revealed significant associations between certain lifestyle factors and BDs. Maternal age over 30 years was found to be significantly associated with BDs, while other studies have reported higher rates among younger mothers. The education level of parents, with higher education being protective against BDs, and parental illiteracy being significantly associated with BDs, align with findings from other studies. Additionally, low maternal body mass index

(BMI) was significantly associated with BDs in this study, contrary to the association between maternal obesity and adverse pregnancy outcomes observed in developed countries. The prevalence of BDs was also higher in rural areas, potentially due to toxic environmental exposures such as fertilizers and insecticides. The association between rural residency and BDs should be further explored in future research. While a history of hypertension (HTN) and diabetes mellitus (DM) did not emerge as significant risk factors in this study, multivariate analysis indicated that DM was a significant risk factor for BDs. Prolonged sunlight exposure and paternal smoking were also found to be significantly associated with BDs. The use of solid fuels for cooking, prevalent in Bangladesh, may contribute to low maternal BMI and potentially cause birth defects. Furthermore, inadequate maternal intake of fish, meat, egg, and milk was significantly associated with BDs. These intriguing findings highlight the need for further research with more robust study designs to confirm the associations between parental periconceptional lifestyle factors and birth defects. Future studies should explore these factors in greater depth and expand our understanding of their underlying mechanisms.

7. Recommendation

As most of the pregnancy in our country is unplanned more importance should be given to the pre-conceptional and periconceptional care for every woman of reproductive age including maternal nutrition with a balanced diet, immunization against Rubella, regular antenatal checkup, avoidance of environmental as well as household toxins and folic acid supplementation during the periconceptional period.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

Ethical Approval

The study was approved by the institutional ethics committee.

Orchid ID

Nusrat Shams: https://orcid.org/0009-0006-8477-2092

References

[1] Sadler TW, 1995. Langman's medical embryology. 7hed. Philadelphia (USA): Lippincot Willium & Wilikins, p23-143.

[2] World Health Organization (WHO), 3-6 October 2011. Training Program on Surveillance and Prevention of Birth Defects and Preterm Births International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), Centers for Disease Control and Prevention (CDC), Geneva, Switzerland.

[3] Patel ZM, Adhia RA, 2005. Birth defects surveillance study. Indian J Pediatr, 72: 489-91.

[4] Boris AW and Biesecker LG, 2009. Dysmorphology. In: BehrmanRE, Klingman RM, Jenson HB, Stanton BF. Nelson text book Pediatrics. Vol. 1.18 ed. Phiiadeiphia (USA): Saunders Elsevier, p 786-93.

[5] Dolk H, 2005. Review EUROCAT: 25 years of European surveillance of congenital anomalies. Arch Dis Child Fetal Neonatal Ed, 90: F355-F358.

[6] Bhat BV, Kumar MR, 1996. Perinatal mortality trends in a referral hospital in India-Need for introspection. Indian J Maternal and Child Health, 7: 313-17.

[7] Chaturvedi P, Bancrjec KS, 1989. Spectrum of congenital malformations in the newborns from rural Maharash. The Indian J Pediatr, 56: 501-7.

[8] Agarwal SS, Singh PS, 1991. Prevalence and spectrum of congenital malformations in a prospective study at a teaching hospital. Indian J Med Res, 94: 413-9.

[9] Chowdhury K, Moiiah MAH, Chowdhury AM, Parvin R, Begum M, 2013. Pattern and Frequency of Congenital Anomalies among Newborn: A Hospital Based Study. J Bangladesh Coll Phys Surg, 31 (2): 84-87.

[10] Islam MN, Siddika M, Bhuiyan MKJ, Chowdhury AM, 2013. Pattern of Congenital Anomalies in Newborns in a Tertiary Level Hospital in Bangladesh. Journal of Surgery Pakistan (International), 18 (1): 32-36.

[11] Khatun F, Begum F, Akter N, Zaman SMM, 2011. Major Congenital Malformations among the Newborns in BSMMU Hospital. Bangladesh Medical Journal, 40 (1): 7-12.

[12] Khanum S, Noor K, Kawsar CA, 2004. Studies on congenital abnormalities and related risk factors. Mymensingh med J, 13 (2): 177-80.

[13] Christianson A, Howson CP, Modell B, 2006. March of Dimes Global Report on Birth Defects the Hidden Toll Of Dying and Disabled Children White Plains, New York.

[14] Concise Oxford English Dictionary. 10th ed revised. New York: Oxford University Press; 1999. Lifestyle; p-820.

[15] Illustrated Oxford English Dictionary. revised ed. New York: Oxford University Press; 2003. Lifestyle; p-468.

[16] Dorland's Illustrated Medical Dictionary. 28th ed; Philadelphia: WB Saunders; 1994. Conception. p-365.

[17] Penchaszadeh VB, 2002. Preventing Congenital Anomalies In Developing Countries. Community Genet, 5: 61-69.

[18] WHO SEARO, 2013. Birth Defects in South-East Asia A public health challenge. India.

[19] Raza MZ, Asfandyar S, Ahmed SS, Ali S, Naqvi SMA, 2012. Risk factors associated with birth defects at a tertiary care center in Pakistan. Italian Journal Of Pediatrics, 38: 68-75.

[20] Zhang X, Li S, Wu S, Hao X, Guo S, Suzuki K et al, 2012. Prevalence of birth defects and risk-factor analysis from a population-based survey in Inner Mongolia, China. BMC Pediatrics, 12: 125 -31.

[21] Costa CM, Gama SG, Leal MC, 2006. Congenital malformations in Rio de Janeiro, Brazil: prevalence and associated factors. Cad Saude Publica, 22 (11): 2423-31.

[22] Gaillard, R., 2015. Maternal obesity during pregnancy and cardiovascular development and disease in the offspring. *European journal of epidemiology*, *30*, pp. 1141-1152.

[23] Yazdy MM, Liu S, Mitchell AA and Werler MM, 2010. Maternal Dietary Glycemic Intake and the Risk of Neural Tube Defects. Am J Epidemiol, 171: 407-414.

[24] Waller DK, Shaw GM, Rasmussen SA, Hobbs CA, Canfield MA, Siega-Riz AM, 2007. Prepregnancy Obesity as a Risk Factor for Structural Birth Defects. Arch Pediatr Adolesc Med, 161 (8): 745-750.

[25] Ali WHAB, Balaha MH, Moghannum MSA, Hashim I, 2011. Risk factors and birth prevalence of birth defects and inborn errors of metabolism in Al Ahsa, Saudi Arabia. Pan African Medical Journal, 8: 14-18.

[26] Lebby KD, Tan F and Brown CP, 2010. Maternal Factors and Disparities Associated with Oral Clefts. Ethn Dis, 20 (Suppl 1): 146-9.

[27] Thulstrup AM and Bonde JP, 2006. Maternal occupational exposure and risk of specific birth defects. Occupational Medicine, 56: 532-543.

[28] Shawky RM, Sadik DI, 2011. Congenital malformations prevalent among Egyptian children and associated risk factors. The Egyptian Journal of Medical Human Genetics, 12: 69-78.

[29] Suzan LC, Shaw GM, Yang W, Abrams B and Lammer EJ, 2007. Maternal Stressful Life Events and Risks of Birth Defects. Epidemiology, 18 (3): 356-361.

[30] Benedum CM, Yazdy MM, Mitchell AA. and Werler MM, 2013. Risk of Spina Bifida and Maternal Cigarette, Alcohol, and Coffee Use during the First Month of pregnancy. Int. J. Environ. Res. Public Health, 10: 3263-3281.

[31] Hackshaw A, Rodeck C, Boniface S. Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. Human reproduction update. 2011 Sep 1; 17 (5): 589-604.

[32] Li Z, Zhang L, Ye R, Pei L, Liu J, Zheng X, 2011. Indoor Air Pollution From Coal Combustion and the Risk of Neural Tube Defects in a Rural Population in Shanxi Province, China. American Journal of Epidemiology: 1-8.

[33] WHO, 2007. Impact of Tobacco-related Illness in Bangladesh. New Delhi.

[34] Rahman MO and Azad KMAK, 2009. Low Maternal Nutritional Status in Bangladesh: Solid Fuels and Rural Residence Matters but NGO Membership Does Not. 12ih ASCON, 014 (199).

[35] Kim A, Kim SR, Yang SH, Han JY, Kim MY, Yang JH et al, 2002. multi-center Study for Birth Defects Monitoring Systems in Korea. Korean J Obstet Gynecol, 45 (11): 1924-1931.

[36] Gupta PC, Sreevidya S, 2004. Primary care Smokeless tobacco use, birth weight, and gestational age: population based, prospective cohort study of 1217 women in Mumbai, India. BMJ; 1-5. [doi: 10. 1136/bmj.38113.687882. EB].