DYSLIPIDEMIA IN PREGNANCY MAY CONTRIBUTE TO INCREASED RISK OF NEURAL TUBE DEFECTS - A PILOT STUDY IN NORTH INDIAN POPULATION

Supriya Gupta**, Sarika Arora, S S Trivedi* and Ritu Singh**

Department of Biochemistry, GB Pant Hospital, New Delhi. Departments of *Obstetrics & Gynaecology and **Biochemistry, Lady Hardinge Medical College & Associated Hospitals, New Delhi, India.

ABSTRACT

Neural tube defects are congenital structural abnormalities of the brain and vertebral column resulting from improper or non-timely closure of the neural tube. Prevalence of neural tube defects is reported to be higher among women with diabetes mellitus and obesity. This study was designed to investigate the relation between the presence of dyslipidemia in antenatal patients and the risk of fetal neural tube defects. The present study was an observational, cross-sectional study involving 129 pregnant women in 16 to 18 weeks gestation period. Of these, 80 women had normal pregnancies and 49 were clinically high-risk cases for neural tube defects. Fasting blood samples were analyzed for blood sugar and lipid profile by enzymatic assay and alpha-fetoprotein levels using Enzyme Immunoassay. Alpha-fetoprotein (AFP) values were converted to Multiples of Median (MoM) appropriate for the gestational age. Based on AFP values, women were labeled as screen negative (AFP < 2 MoM, n = 102) and screen positive (AFP > 2 MoM, n = 27). Screen positive women were further evaluated by ultrasound and 21 women were found to carry a neural tube defects positive pregnancy. Statistical analysis was done on SPSS software. Body weight of the women showed a significant positive correlation with serum triglycerides, plasma sugar and AFP MoM values. A significant difference was observed in serum cholesterol levels (p = 0.038), triglycerides (p = 0.001) and plasma sugar levels (p = 0.002) between normal women and those with neural tube defects positive pregnancy. The Odds ratio for neural tube defects risk in dyslipidemic cases was 24.23 (CI 4.73 – 148.60) with a relative risk of 12.12. Dyslipidemia especially hypertriglyceridemia was found to be significantly associated with fetal neural tube defects.

KEY WORDS

Neural tube defects, Dyslipidemia, Alpha Feto Protein, Multiples of Median.

INTRODUCTION

Neural tube defects (NTD) are congenital structural abnormalities resulting from a defect in any part of the neuraxis. The presentations vary from anencephaly, encephalocele, spina bifida occulta or cystica. They comprise one of the most common and severe congenital malformations (1). The prevalence of NTD from different parts of India has been reported to vary from 0.5 to 11 per 1000 births (2-4). In general the prevalence of NTD in north Indian states like Punjab, Haryana, Delhi, Rajasthan, UP and Bihar has been much higher (3.9-9.0/1000) compared to eastern, western and southern parts of the country (0.5-2.64/1000) (4,5).

The development of neural tube is a multi-step process strictly controlled by genes and modulated by a host of environmental factors. Despite considerable advances in the understanding of Neural Tube Defects, etiology in many cases still remains unknown. It is widely accepted that interplay of genetic and environmental factors may result in neural tube defects (6). The etiology of NTD is very heterogeneous, with the impact of a given risk factor varying by the types of NTD and the presence or absence of other defects (7). The recurrence risk for NTD is approximately 3-4%, with the risk being slightly higher if the prior infant or fetus had anencephaly (8). However, 95% of

Address for Correspondence:
Dr. Sarika Arora
Department of Biochemistry
418, Academic Block, G.B. Pant Hospital,
New Delhi-110002, India.
M: 91-9811266400.
E-mail: sarikaarora08@rediffmail.com
infants with NTD are born to parents with no family history of the defect, thereby increasing the importance of search for risk factors for development of neural tube defects. The neural tube closes by approximately the 28th day of gestation (9), so any potential exposures suspected to have caused an NTD would have to have occurred within the first month of gestation.

A number of studies have reported maternal age risk for NTD to be U-shaped, i.e., highest among youngest and oldest women, while other studies have found a decreased risk with increasing age (10, 11). Maternal weight has been associated with NTD risk. Obesity has been linked to increased NTD rates (12). However, another study failed to find any association between maternal weight and NTD risk (13). A few studies have indicated an increased risk of NTD in women with diabetes (14), although other studies reported no association between maternal diabetes and NTD (15). Diabetic pregnancies may be related to the occurrence of hyperlipidemias in late phases probably due to increased insulin resistance (16).

Over the last several decades, women carrying a fetus with an open NTD have been found to have elevated maternal serum levels of alpha-fetoprotein (AFP) (17). Prenatal screening of these substances, along with ultrasonography has allowed NTD to be identified in utero. However, in India due to illiteracy, lack of awareness and cost constraints, screening for NTD is not yet included in routine screening. Hence the prevalence of neural tube defects and their resulting economic and social burden still remains high compared to western population. Studies from various birth defects surveillance systems have found that, in regions where elective termination is allowed, prenatal diagnosis and elective termination reduce the birth prevalence of NTD, with the reduction being greater for anencephaly than for spina bifida (10, 11, 18). Thus this study aimed at screening of the prenatal suspected high-risk patients for NTD using maternal serum AFP. Since, obesity, body weight and elevated blood sugar levels are linked to dyslipidemia; we evaluated its association with the risk of development of NTD in fetus.

MATERIALS AND METHODS

A total of 129 pregnant women in 16 to 18 weeks gestation period were selected from the wards and antenatal clinics of Smt Sucheta Kripalani Hospital, New Delhi that is a tertiary care referral hospital for antenatal patients. Of these, 80 women had normal pregnancies. 49 women were suspected high-risk cases for NTD on clinical evaluation. These women either had a family history or previous suspected history of NTD or had pregnancy complicated by medical disorders like diabetes, or history of drug intake like antiepileptic drugs e.g. valproate or with a history suggestive of nutritional deficiency and recurrent infections. The institutional ethical committee approved the study and the women were included after a written informed consent. Patients with other conditions that may increase AFP levels (hepatitis, cirrhosis, hepatocellular carcinoma and germ cell cancers) were excluded from the study. 5 ml fasting venous blood sample was collected from each patient and divided into three parts. 1.0ml for AFP, 1.0 ml in Sodium Fluoride for plasma glucose and 3.0ml in plain vial for routine biochemical tests. Plasma glucose was estimated by Glucose-oxidase method and lipid profile (serum cholesterol and triglycerides) was done by enzymatic method on Synchron CX9 using kits and calibrators from Randox. 0.5 ml of serum was stored in duplicate at -20°C until analysed for alpha-fetoprotein levels by solid phase Enzyme Linked Immunosorbent Assay using UBI MAGIWEL kit. AFP values obtained for each patient and control sample were converted to Multiples of Median (MoM) appropriate for the gestational age. AFP values less than 2 MoM were considered as screen negative and those more than 2 MoM were considered to be screen positive and further evaluated by ultrasonography. For further evaluation of biochemical and physiological parameters, the women were divided into the NTD positive pregnant cases and the control group (negative screen test and/or negative ultrasound scan). Data are expressed in Mean ± Standard Error of Mean. Maternal characteristics were compared between groups using a non-paired t-test for continuous variables, a median or Wilcoxon rank-sum test for non-parametric data, and the chi-square test or Fisher’s exact test for categorical data. Odds ratio and 95% confidence interval were derived for comparing women with 2 to 3 features of metabolic syndrome with women having none of the features. Means and standard error of mean were computed and compared using an unpaired t-test. Association of NTD risk with physical and biochemical parameters was assessed using Pearson’s correlation coefficient. Statistical analysis was carried out using SPSS for windows 12.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

In this study, we screened 129 pregnant women for NTD using Maternal Serum AFP (MSAFP). Out of the total 129 women screened, 27 women had AFP MoM values more than 2 and were considered screen positive. Screen positive women included 21 women from the high risk group and 6 women were from the normal pregnancy group. Out of the 49 women in high-risk pregnancy group, 21 women turned out to be screen