CERVICAL DYSPLASIA IN JAMAICAN WOMEN: LIFESTYLE AND GENETIC FACTORS

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ABSTRACT

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The effects of lifestyle and genetic factors in the development of cervical dysplasia were examined in 236 Jamaican women recruited consecutively from the UHWI, Colposcopy clinic and 102 women with normal Pap smears from the Gynaecology clinic served as controls. All the women gave written, informed consent and donated 10ml of blood for the study. They were interviewed privately on their lifestyle practices and use of hormonal contraceptives. Genomic DNA was prepared from buffy coats. The human leucocyte antigen (HLA) typing and detection kits (Dynal Biotech) were used for HLA class I- A & -B, HLA class II -DRB1and -DQB1in cases and controls. PCR and RFLP were used to genotype Single Nucleotide Polymorphisms (SNPs) in the Tumour Necrosis Factor (TNF-α), Heat Shock Proteins (Hsp70-2) and Tumour Suppressor Proteins (p53) genes. The data generated were analyzed using χ^2 test, ANOVA and logistic regression using the SPSS version 12.

This study revealed that socio-economic status, alcohol consumption, parity and number of biological fathers were statistically significantly associated with development of cervical dysplasia compared to healthy controls (p =0.020, 0.019, 0.005 and 0.008 respectively). The association with parity and

alcohol consumption were independent risk factors. Zero parity was found to be a protective factor in controls compared to cases (p = 0.000). Severity of disease was associated with number of sexual partners. There were more women in the controls group who had Pap smears done compared to women with cervical dysplasia (p = 0.0001). The current and / or past exposure to hormonal contraceptive use by either the pill or injection, alone or in combination with other methods was statistically significantly higher in the women with cervical dysplasia. In multivariate analysis with age as a co-variate, use of hormonal contraceptive was associated both with disease and the severity of the disease (OR 2.04, CI 1.18, 3.50; p = 0.010 and OR 2.21, CI 1.07, 4.57; p = 0.033) respectively. Exposure to hormonal contraceptive for more than 4 years conferred more risk for disease and severity of disease. HLA-Class I-A- B antigens were not statistically significantly associated with disease. HLA- DRB1 and DQB1 showed no significant difference in their distribution between women with cervical dysplasia and healthy controls.

The distribution of the tumour necrosis factor alpha (TNF-α) 308 allelic variant was significantly different between cases and controls: 20.3% among the cases had the A (mutant) allele compared to 7.7% of the controls, p = 0.0001. There were statistically significant differences in genotypes and allelic frequencies among controls, cases, and each disease status (p = 0.036, 0.001, 0.000, and 0.001). Regression analysis showed an association of disease with the variant allele, (genotype: OR= 2.7, CI 1.5, 4.71; allele: OR = 2.7, CI = 1.49, 5.08). The association remained significant when parity, alcohol

consumption and hormonal contraceptive use was added (genotype: OR = 2.4, CI 1.34, 4.29; allele: OR = 2.3, CI 1.22, 4.52). In low (LGSIL) and high risk (HGSIL) cervical dysplasia, TNF-α was significantly associated with severity of disease (χ^2=7.9; p=0.019).

The genotype and allelic variant of Hsp-70-2 did not differ significantly between the women with cervical dysplasia as a group and healthy normal controls (p = 0.428, p=0.730), no significant differences were observed between categories of cervical dysplasia when cases were classified according to the Bethesda classification.

There was a statistically significant decrease in the p53 arginine variant in women with CIN III compared to healthy controls (p= 0.037; OR, 0.56, 95% CI 0.34- 0.94) and a statistically significant increase in the p53 proline variant in women (p = 0.037; OR, 1.78; 95% CI 1.07-2.94). The arginine variant was also significantly decreased in women with high grade squamous intraepithelial lesions (HGSIL) compared to low grade squamous intraepithelial lesion (p = 0.028,; OR 0.61, 95%CI 0.40-0.93) and the proline variant increased (p = 0.028, OR, 1.65, 95% CI 1.078 – 2.513).

The blood groups O and A were the most frequently occurring ABO blood groups in cases and control (54.2%, 26.1 % vs 54.1, 25.9; χ^2 0.019, p=0.99). There were no significant differences in the distribution of the blood groups in cervical dysplasia and healthy control subjects. The analysis of the blood groups in different stages of cervical dyspalsia and healthy controls showed no statistically significant association (χ^2 6.5; p= 0.89).

Some lifestyle factors and hormonal contraceptive use are associated with cervical dysplasia in Jamaican women. The TNF-alpha SNP polymorphism showed statistically significant association with all stages of cervical dysplasia independent of the HLA-class I, and II haplotypes. The p53 codon72 genotype and variant allele was associated with CIN III and HGSIL when compared to healthy controls and LGSIL subjects.