Cervical Intraepithelial Neoplasia In Egyptian Patients

A Histopathological And Statistical Study

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1. Abstract

The purpose of this study was to detect the incidence of the various precancerous lesions of the cervix (CIN for the ectocervix and CGIN for the endocervix) and correlate them with the different histopathological lesions detected.

CIN cases were found in 13% of the cases, while CGIN cases were found only in 6 % of the cases. The incidence of CIN I and CIN II cases were generally lower than that detected in Usa , Europe and Asia , however CIN III cases were found to be nearly within the same range.

Concerning CGIN cases, their incidence were nearly the same like that detected in other countries.

Koilocytosis were mostly found to be associated with CIN I lesions, and nearly not found with CIN III lesions.

Endometrial hyperplasia without atypia was closely associated with both CIN and CGIN cases.

Endocervical stromal inflammation was detected in all the cases of CGIN, probably sharing in causation.

Nabothian cysts were detected almost in all cases examined. CIN and CGIN lesions were poorly associated with each other.

Key words: CIN and CGIN.

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3. List of abbreviations

CIN I = Cervical Intraepithelial Neoplasia grade I

CIN II = Cervical Intraepithelial Neoplasia grade II

CIN III = Cervical Intraepithelial Neoplasia grade III

LSIL = Low-grade Squamous Intraepithelial Lesion

HSIL = High-grade Squamous Intraepithelial Lesion

L.I = Labeling Index

HPV = Human Papilloma Virus

t = value of t-test

F = F ratio for ANOVA

X2 = Chi square test

P = P value

P<0.05* = Significant at .05 level

P<0.01** = Significant at .001 level

P>0.05 (NS) = Not significant

Std = Standard deviation

SPSS = Statistical Package for Social Sciences

4. Introduction

Cervical intraepithelial neoplasia (CIN) is predominantly a disease of women in their reproductive years with a large population impact and risk factors characteristic of a sexually transmitted disease (STD) (Sadeghi SB, Sadeghi A and Robboy, 1988).

The clinical scope and epidemiology of squamous intraepithelial lesions (SIL) or CIN has undergone dramatic changes over the past few decades. SIL (CIN) appears to be becoming increasingly common. A review of cervical biopsies over a ten-year period found that the prevalence of cytological evidence of low-grade SIL (CIN I) increased from 0.6% in 1978 to 5.6% in 1988 (Evans and Dowling, 1990). The mean age at diagnosis of high-grade SIL (CIN II, III) is decreasing, as both the incidence and prevalence of high-grade SIL (CIN II, III) increase in teenagers and women under 30 (Cramer and Cutler, 1974). Cytological evidence of high-grade SIL (CIN II, III) can now be found in women under the age of 15 years and the age-specific incidence for CIN III currently peaks in the 25-29 year old group and decreases with advancing age (Schiffman, 1992). The prevalence of low-grade SIL (CIN I) and high-grade SIL (CIN II, III) combined in teenagers and young adults aged 15-19 years is 18.8 per 1000 (Sadeghi SB, Hsieh and Gunn, 1984).

Although the incidence in Iraq is relatively low, as in most Islamic countries (i.e. making approximately 4% of all female cancer), yet the cases usually present in advanced stages with poor prospects of cure. Hence the feasible control strategy seems to encourage women for case finding and early detection. CIN was diagnosed in 9.3% of the examined specimens, the majority of which were CIN I (82.5% of total CIN), those had a close relationship with chronic cervicitis. CIN II were observed in 17 patients (i.e. 1.2%) while changes consistent with CIN III were detected only in 6 (0.4%). Chi-Square statistics showed that squamous metaplasia and the Trichomonus vaginalis were significantly more common in patients with CIN (Alwan, 2000).

These epidemiological changes have been attributed to changes in sexual behavior patterns and corroborate previous epidemiologic data suggesting a direct causal relationship between sexual activity and the pathogenesis of cervical neoplasia. They also underscore the importance of performing cytological screening in sexually active teenagers.

5. Aim of the work

The aim of this work is a histopathological and statistical study of cervical Intraepithelial Neoplasia (squamous and glandular) in the Egyptian Patients with reference to associated lesions.

6. Review of literature

6.1 Embryology & Histology of the cervix

The cervix uteri is differentiated into two segments, the ectocervix that area covered by stratified squamous epithelium, and endocervix lined by high columnar mucous secreting elements. The ectocervix is derived from the invading epithelium of the urogenital sinus, or possibly the vaginal plate epithelium of the united mesonephric ducts. The endocervix is of paramesonephric origin. Embryologically, there is definable secretory activities in the endocervical glands during late embryonic life (Corliss, 1976).

Histologically, the mature nonkeratinized squamous epithelium of the ectocervix is divided into three zones: the basal or germinal cell layer, which is responsible for continuous epithelial renewal; the midzone or stratum spinosum, the dominant portion of the epithelium; and the superficial zone, containing the most mature cell population (Foraker and Marino, 1961).

The basal zone is composed of one or two layers of elliptical cells with scanty cytoplasm and oval nuclei characteristically oriented

perpendicular to the underlying basal lamina (pallisade). Epithelial regeneration is the major function of the basal cells.The lower third of the midzone contains larger cells than the basal variety, with a comparatively more abundant cytoplasm, they are also called parabasal cells. They may occasionally exhibit mitotic divisions.(kurman 1994)

The upper portion of the midzone is occupied by cells that are involved in a process of ascending maturation, during which there is a gradual increase in the volume of the cytoplasm. Nuclear size, however, remains constant up to the most superficial cell level. These cells are referred to as intermediate cells when exfoliated. They do not divide, and have abundant PAS-positive, diastase-labile intracellular glycogen which is responsible for the clear “vacuolated” appearance of their cytoplasm (Kurman, 1994).

The superficial zone forms the most differentiated compartment of the squamous epithelium. These cells are flattened and have a larger area of cytoplasm and smaller pyknotic nuclei than the underlying intermediate cells (Kurman, 1994).

The mucosa of the cervical canal (endocervix) is composed of a single layer of mucin-secreting, columnar epithelium that lines both the surface and the underlying glandular structures, which are called compound or tubular endocervical glands. Because of the complex architecture of these clefts, or grooves, including oblique, transverse and longitudinal arrangements, they appear as isolated glands in histological sections (Ferenczy, 1982).

The squamocolumnar junction of the cervix is defined as the border between the stratified squamous epithelium and the mucin-secreting columnar epithelium of the endocervix. There are two different squamocolumnar junctions. One is termed the original squamocolumnar junction and is the site at which the squamous covering of the ectocervix meets the endocervical columnar epithelium at the time of birth.At about the age of one year, the cervix begins to elongate. This result in migration of the squamocolumnar junction towards the external os (Linhartova, 1978).

At the time of menarche or during pregnancy both the uterus and the cervix enlarge. Enlargement of the cervix is accompanied by alterations in its shape, which result in more of an “eversion” or rolling outwards of

endocervical columnar epithelium. As a result, in most women during the reproductive period, cervical ectopy is present, and the size of ectopy is most extensive in younger women (under 20 years of age) after the first pregnancy (Robboy, Taguchi and Cunha, 1982).

Over time, the columnar epithelium that composes the cervical ectopy is remodeled and replaced by metaplastic squamous epithelium. The histological squamocolumnar junction moves toward the ectocervical os. This newly formed squamocolumnar junction is called the *physiologic or functional* squamocolumnar junction, whereas the original squamocolumnar junction usually is quite abrupt. The junction between the columnar and squamous epithelium at the physiologic or functional squamocolumnar junction can be either abrupt or gradual. The region between the neonatal original squamocolumnar junction and the post pubertal functional squamocolumnar junction is termed the transformation zone (Richart, 1973).

Squamous metaplasia is the replacement of the mucin-producing columnar epithelium of the endocervix by stratified squamous epithelium and appears to occur by two different mechanisms. One mechanism consists of direct ingrowth from the squamous epithelium nearby the

columnar epithelium, a process referred to as squamous epithelialization. The second mechanism is a proliferation of reserve cells of the endocervical epithelium that differentiate into squamous epithelium (Kurman, 1994).

The transformation zone is of particular importance, since it is the area where most of cervical dysplasias and neoplasia arise (Richart, 1973; and Guijon et al., 1985). During the childbearing ages and pregnancy the transformation zone is located mostly on the exposed portion of the cervix, consequently the vast majority of cervical neoplasia can be removed for histologic diagnosis by punch biopsy because the extension and limits of cervical intraepithelial neoplasia coincide with the distribution of the transformation zone (Richart, 1973).