

Quantitative Alterations of Immunoglobulins In Human Cervicovaginal Secretions

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ABSTRACT

The human genital tract has a local immunological defense mechanism which is independent of systemic immunity, IgA & IgG are the predominant immunoglobulins which protect the female reproductive tract against microbial invasion. The concentrations of IgG, IgA and IgM were measured in the cervico-vaginal secretions of 43 women with normal vaginal discharge (NVD), 36 cases with non-specific vaginitis (NSV), 37 pregnant women, 26 IUD users, 7 women on 42nd postpartum day, and 29 hysterectomized women together with 32 cases serum level for comparison.

The serum IgG/IgA ratio was 5.3 ± 0.3 (mean $\pm$ SE), while the cervicovaginal secretion was 12.1 ± 1.7 . In 28-days normal menstrual cycle, IgG during luteal phase was higher than that during follicular phase; IgA level was markedly decreased at the ovulation. In non-specific vaginitis (NSV), IUD & pregnant groups, IgG was significantly increased compare to IgA; but in the postpartum women, IgA was significantly increased. In hysterectomized women, IgA level was markedly decreased. This fact might mean that IgA was produced predominantly from upper genital tract. IgM was found only in trace amount in all groups tested, in the cervicovaginal secretions.

Key words: Immunoglobulins, cervicovaginal secretions.

Investigation of the products of external secretory glands of the human body has revealed that some of them secrete antibody locally. Although the presence of antibodies in these secretions may be due to passive diffu-

sion of circulation plasma components, recent evidence has suggested that local appearance of antibody may be due to a mechanism independent of circulating antibody. The female reproductive tract is considered to be part of

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the secretory immune system^(1,2). Immunoglobulins, IgA and IgG, are the predominant Igs in external secretions that protect the female reproductive tract and other mucosal surfaces of the body against microbial invasion⁽³⁾. It is well known that estrogen and progesterone modify the epithelium and the consistency of the cervical mucus and affect secretions of the genital tract⁽⁴⁾. It seemed interesting to determine IgG, IgA and IgM levels in cervico-vaginal secretions of normal patients through various phases of menstrual cycle. The secretions of patients with vaginal infection, IUD user, pregnancy, postpartum, and hysterectomized women were also measured and compared.

MATERIALS AND METHODS

A total of 210 cases were examined, and the concentrations of IgG, IgA & IgM were compared with each other. Thirty two cases of serum immunoglobulins were taken as control group, the others were cervico-vaginal secretions. Forty three cases were normal vaginal discharge (only 1 or 2 polymorphs per high power field on wet smear) (age 16-40, mean age: 30.1), 36 cases were non-specific vaginitis which wet smear showed numerous polymorphs and clue cells (age 22-46, mean age: 31.4). Secretions were also collected in 37 pregnancies, (age 20-38, mean age: 28.6), 26 IUD users, (age 22-40, mean age: 31.9), 7 42-days postpartum (age 26-36, mean age: 29.9), and 29 hysterectomized women of at least half year (age 28-54, mean age: 43.3). (Table 1) Secretions were obtained by thoroughly washing the cervix and vagina with 2 ml of sterile normal saline^(7,8). After fluid collection and

Table 1 The case number and mean age of each group.

	n	mean age
Serum	32	31.3
NVD	43	30.1
NSV	36	31.4
Pregnancy	37	28.6
Postpartum	7	29.9
IUD	26	31.9
Hysterectomized	29	43.3

Total 210
 NVD: normal vaginal discharge
 NSV: nonspecific vaginitis
 IUD: intrauterine device

centrifugation at 1,000xg for 10 minutes, supernatants were stored at -20°C.

Measurement of IgG, IgA & IgM. Beckman immunochemistry system analyzer II was employed with rate nephelometric measurement for IgG, IgA & IgM determination. The statistic significance was calculated by student's t test.

RESULTS

The immunoglobulin concentration in serum and cervicovaginal secretions varied considerably from one individual to another. (Table 2) The IgG/IgA ratio of serum was 5.3 ± 0.3 and of the normal vaginal discharge (NVD) was 12.1 ± 1.7 . During the menstrual cycles, IgG of cervicovaginal secretions was slightly increased in the luteal phase and the IgG/IgA ratio was also significantly increased in the luteal phase. In this study, we found that IgA concentration was markedly decreased at the ovulation. (Table 3) In the cases of nonspecific vaginitis, IgG level was 16.7 ± 2.3 mg/dl, while IgA was 8.9 ± 3.6 mg/dl and IgG/IgA ratio was 24.9 ± 9.0 . During

Table 2 The concentrations of IgG, IgA & IgM of serum and normal Vaginal discharge

	IgG mg/dl mean $\pm$ SE	IgA mg/dl mean $\pm$ SE	IgM mg/dl mean $\pm$ SE	IgG/IgA
Serum (n= 32)	1,067.8 $\pm$ 65.8	210.1 $\pm$ 11.9	166.9 $\pm$ 13.7	5.3 $\pm$ 0.3
NVD (n= 43)	5.5 $\pm$ 0.6	3.1 $\pm$ 1.9	0.3 $\pm$ 0.1	12.1 $\pm$ 1.7

NVD: normal vaginal discharge

Table 3 IgG, IgA & IgM levels (mg/dl) in the cervicovaginal secretions and IgG/IgA ratio during normal menstrual Cycle.

	IgG	IgA	IgM	IgG/IgA
Pre-ovulatory (n= 25)	5.5 $\pm$ 0.8	1.7 $\pm$ 0.9	0.2 $\pm$ 0.02	11.0 $\pm$ 1.9
Ovulation (n= 4)	6.7 $\pm$ 3.0	0.48 $\pm$ 0.2	0.2 $\pm$ 0.06	18.0 $\pm$ 4.7
Post-ovulatory (n= 19)	7.4 $\pm$ 1.2	1.9 $\pm$ 1.3	0.5 $\pm$ 0.2	16.1 $\pm$ 2.2
P value	0.1 $>$ P $>$ 0.05	NS		$<$ 0.05

(P: preovulatory vs. postovulatory)

NS: non-significant

Table 4 Immunoglobulins (mg/dl) of nonspecific vaginitis and pregnant women.

	NSV (n= 36)	P value	Pregnancy (n= 37)	P value
IgG	16.7 $\pm$ 2.3	$<$ 0.005	8.8 $\pm$ 1.1	$<$ 0.005
IgA	8.9 $\pm$ 3.6	0.1 $>$ P $>$ 0.05	8.0 $\pm$ 3.1	0.1 $>$ P $>$ 0.05
IgM	0.4 $\pm$ 0.1	NS	0.6 $\pm$ 0.3	NS
IgG/IgA	24.9 $\pm$ 9.0	$<$ 0.05	15.6 $\pm$ 3.3	NS

NSV: non-specific vaginitis NS: non-significant

P value was compared with normal vaginal discharge shown in Table 2.

pregnancy, immunoglobulins were both increased, however IgG/IgA ratio remained unchanged. (Table 4) During all trimesters of pregnancy, the values of IgG were 8.0 $\pm$ 1.9 mg/dl, 7.4 $\pm$ 2.8 mg/dl, & 9.9 $\pm$ 1.5 mg/dl in 1st, 2nd, & 3rd trimester, the values of IgA were 0.6 $\pm$ 0.1 mg/dl, 1.9 $\pm$ 1.6 mg/dl & 12.3 $\pm$

5.5 mg/dl respectively.

IgG and IgA were significantly increased in the 3rd trimester. (Fig. 1) In the IUD users, IgG level was 14.7 $\pm$ 2.2 mg/dl, IgA level was 8.7 $\pm$ 3.5 mg/dl and IgG/IgA ratio was higher than non-users. In postpartum, IgG and IgA were both significantly increased. (Table 5)

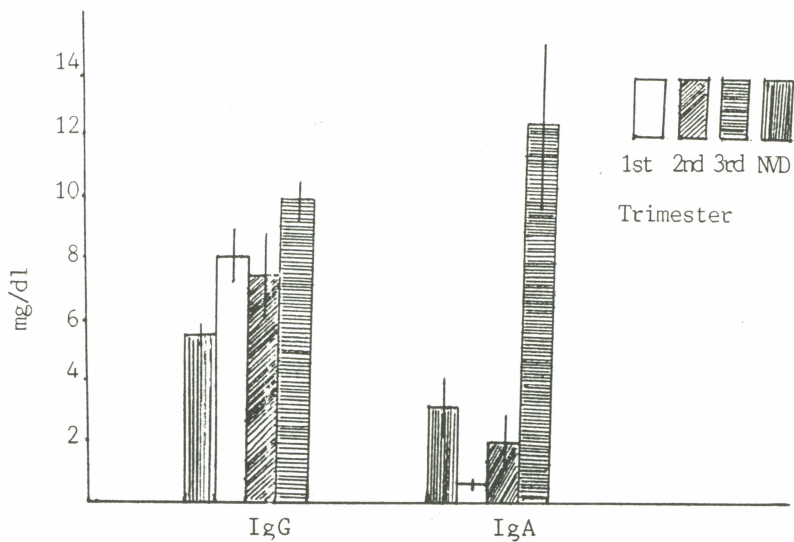


Fig 1. Comparison of IgG & IgA in 3 trimesters of pregnancy and normal vaginal discharge (NVD IgG: 5.5 ± 0.6 mg/dl, IgA: 3.1 ± 1.9 mg/dl, $n=43$)

Table 5 The immunoglobulins (mg/dl) in the cervicovaginal secretions of IUD users & 42 nd day postpartum women.

	IUD	P	Postpartum	P
IgG	14.7 ± 2.2	< 0.005	14.8 ± 3.2	< 0.005
IgA	8.7 ± 3.5	$0.1 > P > 0.05$	25.5 ± 13.5	< 0.005
IgM	0.3 ± 0.06	NS	0.2 ± 0.04	NS
IgG/IgA	23.4 ± 9.2	$0.1 > P > 0.05$	8.2 ± 3.6	NS

(P value was compared with normal vaginal discharge shown in Table 2)

NS: non-significant

Table 6 The comparison of immunoglobulins of normal vaginal discharge and hysterectomized women.

	IgG (mg/dl)	IgA (mg/dl)	IgM (mg/dl)	IgG/IgA
NVD ($n=43$)	5.5 ± 0.6	3.1 ± 1.9	0.3 ± 0.1	12.1 ± 1.7
Hysterectomized ($n=29$)	5.5 ± 0.8	0.75 ± 0.4	0.27 ± 0.04	38.2 ± 7.6
P value	NS	< 0.05		< 0.05

NVD: normal vaginal discharge

NS: non-significant

IgA was found decreased in the vaginal secretions of hysterectomized women. (Table 6)

DISCUSSION

The present study demonstrates that IgG/IgA ratio in serum is 5.3 ± 0.3 and in the cervicovaginal secretions is 12.1 ± 1.7 . From this, it is evident that the lower female genital tract is a locally immunoglobulin producing organ and IgG is the predominant component. IgM is mostly found in the serum and only in trace amount in the cervicovaginal secretions. In the luteal phase, IgG level is higher than in follicular phase (1970 Elestein, 1973 Schaumacher)⁽¹⁴⁾, while the IgA level shows no significant difference (1965 Herve)⁽¹⁴⁾. During ovulation, IgA level is markedly decreased (1970 Elestein, 1973 Schaumacher)^(9,10,14). When the vagina is infected, there is significant increased in IgG and IgA, and the IgG/IgA ratio becomes 24.9 ± 9.0 . When the endometrium has inflammatory change such as presence of an IUD or in the postpartum state, one can find increase in IgG and IgA. In the postpartum state, it is shown that the uterine cavity manifests inflammatory reaction and produces great quantity of IgA. Some workers find "IgA-producing cells" predominate the uterine cervix (Masson & Ferin 1969)⁽¹³⁾ while others have found IgG to be the predominant immunoglobulin in the cervical tissue (Tourville 1970), Pozzuoli (1971) and Lippes (1970)⁽¹³⁾ are able to identify IgA in epithelial cells of the oviduct, endometrium and endocervix^(11,12). During pregnancy, immunoglobulins are also increased, especially in 3rd trimester. IgA is significantly increased which enable the coating of the invading or-

ganisms by IgA agglutination, thus reducing the invasive capacity of the pathogens and also enhance granulocytic phagocytosis which inhibits the growth of microorganism, thus protect the conceptus from infection⁽¹³⁾. When hysterectomized, IgA reduced significantly. This is probably due to the fact that IgA is mainly produced from the upper genital tract at and above the level of cervix uteri.

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子宮頸陰道分泌物免疫球蛋白

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生殖器官具有局部產生免疫球蛋白的功能，其中以 IgG & IgA 較多，它們可保護生殖道免於細菌的侵襲，本研究測量 43 位正常陰道分泌物，36 位非特異性陰道炎，37 位懷孕婦女，26 位裝有子宮內避孕器，7 位產後 42 天，29 位子宮切除的婦女，及 32 位血清的免疫球蛋白。

血清中 IgG/IgA 的比值是 5.3 ± 0.3 ，而子宮頸陰道分泌物的比值是 12.1 ± 1.7 。在 28 天月經週期中，黃體期 (luteal phase) 的 IgG 比濾泡期 (follicular phase) 高，而 IgA 在排卵時有顯著地減少。非特異性陰道炎，裝有子宮內避孕器，及懷孕婦女，IgG 的增加比 IgA 還多，但在產後婦女子宮頸陰道分泌物中 IgA 有特別顯著的增加。在子宮切除的婦女，IgA 有明顯的降低，亦即表示 IgA 最主要的分泌處是由上生殖道出來的。IgM 最主要是在血液中，而子宮頸陰道分泌物僅有微量存在，且隨各種狀況的變化很小。

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