

The Serum Pregnancy Associated α_2 -Glycoprotein Level in Patients with IgA Nephropathy^{*)}

Shunji TOI, Naoki HAMAGUCHI, Koji WADA,
Toshihide TOYOTA, Kanoko HAYASHI, Michiko ARITA,
Koji USUI, Misaki TADA, Noriaki YORIOKA,
Michio YAMAKIDO, Yukio NISHIMOTO and Jyotaro HATA^{*)}

The 2nd Department of Internal Medicine, Hiroshima University School of Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan

**) The 1st Department of Pathology, Hiroshima University School of Medicine*

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ABSTRACT

Serum pregnancy associated α_2 -glycoprotein levels in 51 IgA nephropathy patients (28 males and 23 females) and 46 healthy subjects (31 males and 15 females) were determined by enzyme-immunoassay. The results showed the serum pregnancy associated α_2 -glycoprotein levels to be significantly increased in the IgA nephropathy patients over the healthy subjects in both sexes (males: $p < 0.01$, females: $p < 0.001$). Further, in the male patients, the level was significantly increased in those with proteinuria, also there was a significant negative correlation between the concentration and PSP 15 minute value and GFR. On the other hand, in the female patient group there was a significant positive correlation between serum total cholesterol level.

On the basis of these findings, we presume that the determination of serum pregnancy associated α_2 -glycoprotein level may be useful in assuming the prognosis of IgA nephropathy.

INTRODUCTION

Pregnancy associated α_2 -glycoprotein (referred to here after as α_2 -PAG) is a glycoprotein with a molecular weight of approximately 360,000 which increases in serum during pregnancy, and has been reported to increase also in patients with malignant tumors^{14-18, 20, 22}, Behçet's disease²⁴, rheumatoid arthritis^{11, 13} etc.. However, reports on the serum α_2 -PAG behaviour in chronic glomerulonephritis are still rare. Thus, we undertook review of the serum α_2 -PAG behaviour in IgA nephropathy which is said to have the highest frequency among chronic glomerulonephritis patients.

MATERIALS AND METHODS

The subjects were 51 IgA nephropathy patients (28 males and 23 females), excluding those currently pregnant or who had complication of

malignant tumors. The ages were males 26.2 ± 12.6 and females 22.5 ± 10.1 . As controls, a group of 46 healthy subjects (31 males and 15 females) whose ages were males 21.3 ± 2.6 and females 20.1 ± 1.7 was selected.

Determination of serum α_2 -PAG level was made by enzyme-immunoassay (Fig. 1), and standard curve was shown (Fig. 2). The lower limit of determination was 0.1 $\mu\text{g/ml}$.

RESULTS

As there is a sex difference in α_2 -PAG level, all subsequent review was made by sex.

The serum α_2 -PAG level in male IgA nephropathy patients was $0.93 \pm 1.20 \mu\text{g/ml}$, while that for healthy subjects was $0.23 \pm 0.57 \mu\text{g/ml}$, thus indicating a significant increase ($p < 0.01$). The same for female patients was $14.48 \pm 12.92 \mu\text{g/ml}$, while that for healthy females was $1.99 \pm 1.93 \mu\text{g/ml}$, indicating a significant increase ($p <$

^{*)} 東井俊二, 浜口直樹, 和田浩治, 豊田敏秀, 林加野子, 有田美智子, 碓井公治, 多田みさき, 頼岡徳在, 山木戸道郎, 西本幸男, 幡城太郎: IgA 腎症患者における血清 Pregnancy associated α_2 -glycoprotein

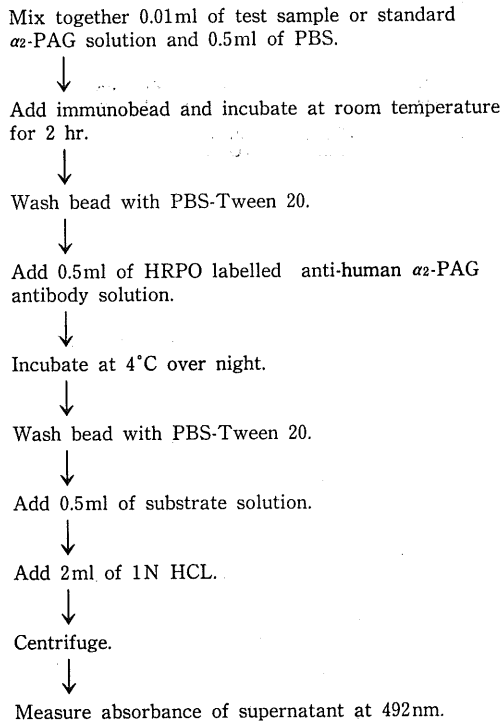


Fig. 1. Method for determination of serum α_2 -PAG level by enzyme-immunoassay

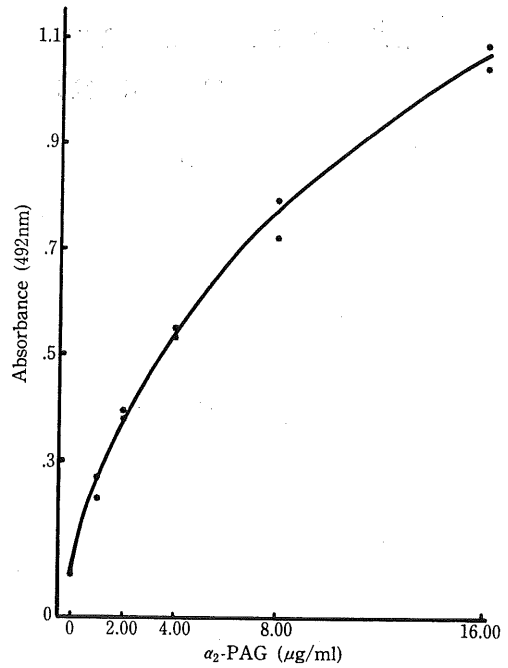


Fig. 2. Standard curve for determination of serum α_2 -PAG level

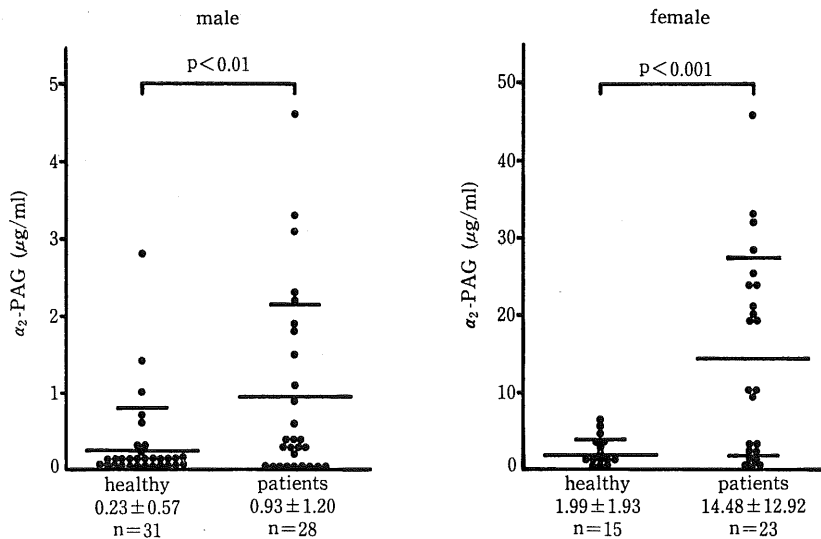


Fig. 3. Serum α_2 -PAG levels in healthy subjects and IgA nephropathy patients

0.001) (Fig. 3).

Next, comparison of serum α_2 -PAG levels was made between the proteinuria positive and negative groups in male IgA nephropathy patients. Results showed that there was a signifi-

cant increase in the positive group as compared with the negative group ($p < 0.05$). However, no significant difference could be demonstrated between the positive and negative groups in the female patients (Fig. 4).

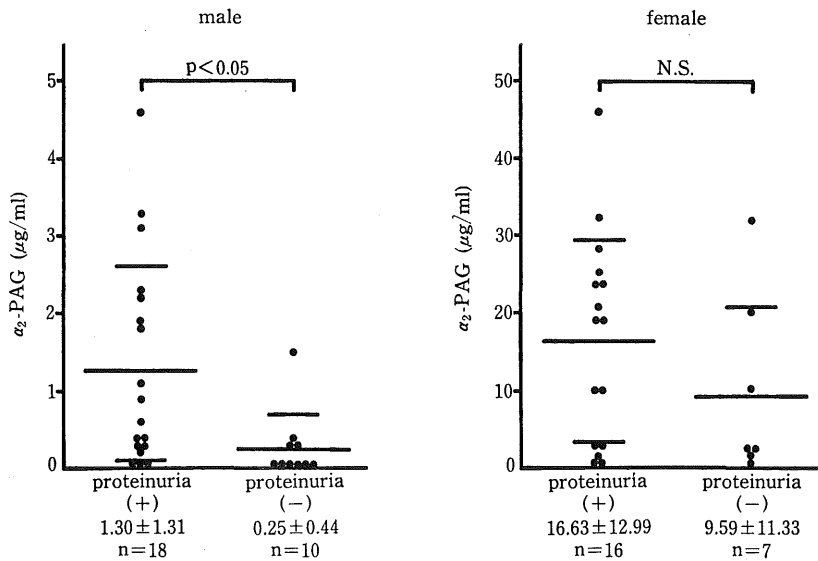


Fig. 4. Serum α_2 -PAG levels in IgA nephropathy patients with proteinuria and without proteinuria

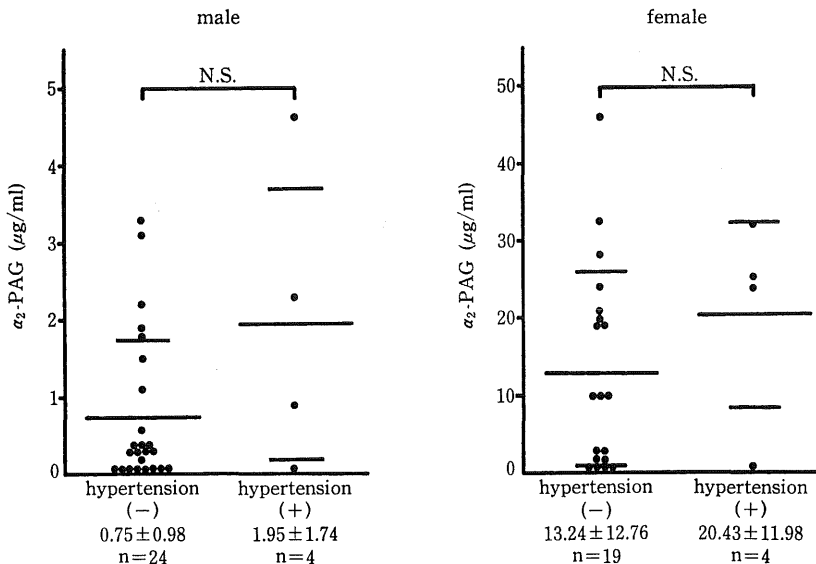


Fig. 5. Serum α_2 -PAG levels in IgA nephropathy patients with hypertension and without hypertension

Further, comparison of serum α_2 -PAG levels between hypertensive and normotensive individuals among IgA nephropathy patients, showed the hypertensives tended to show higher levels in both sexes, but the values were not significant (Fig. 5).

On the other hand, study of the relationship with renal function showed that there was a significant negative correlation between PSP 15 minute value and GFR in male patients (PSP: $p < 0.02$, GFR: $p < 0.05$) (Fig. 6). However, no

such significant correlation was observed in female patients.

Although a significant correlation between serum α_2 -PAG and total cholesterol levels could not be demonstrated in male patients, there was a significant positive correlation in female patients ($p < 0.05$) (Fig. 7).

Further, no significant correlation between serum α_2 -PAG and BUN, serum creatinine, serum uric acid and immunoglobulin levels could be found in both male and female patients.

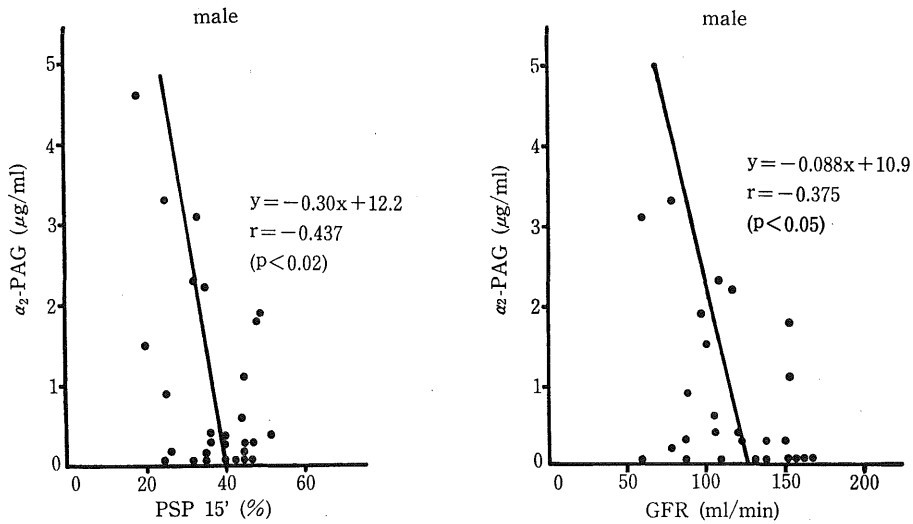


Fig. 6. Correlation between serum α_2 -PAG levels and PSP, GFR in IgA nephropathy patients

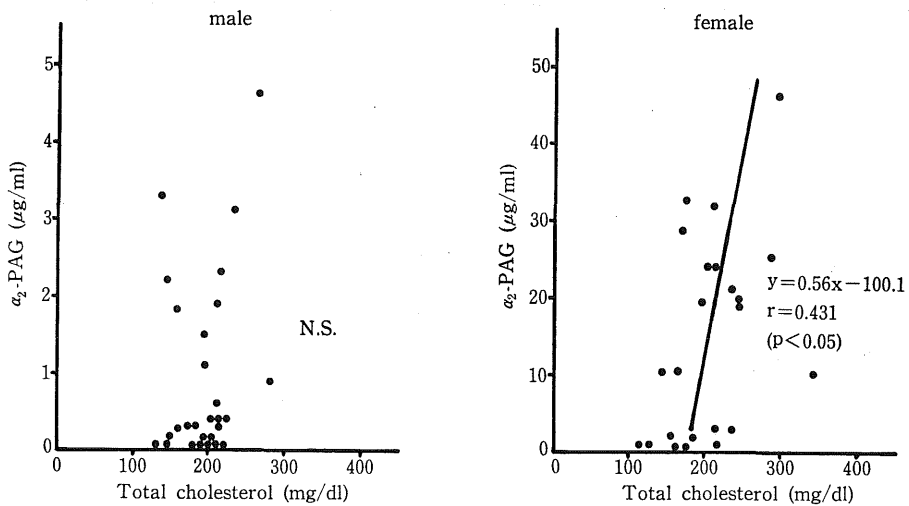


Fig. 7. Correlation between serum α_2 -PAG and total cholesterol levels in IgA nephropathy patients

DISCUSSION

Serum α_2 -PAG is a glycoprotein with a molecular weight of approximately 360,000, glucose content of 12.2% and belongs to the α_2 -globulin zone by electrophoresis with isoelectric points ranging from 4.5 to 4.7, and was first reported by Smithies¹⁹. He made electrophoretic studies of serum of pregnant women using starch gel, and discovered a specific band which was not observed in non-pregnant women or males, and thus named this protein "pregnancy zone protein" (PZP). Subsequently, many researchers have reported on pregnancy proteins under a variety of names^{8,7,12}. In 1971, Bohn⁶ carried

out studies on serum of pregnant women and succeeded in isolating four different types of pregnancy associated proteins. He named them 1) human placental lactogen (HPL), 2) pregnancy specific α_1 -glycoprotein (SP₁), 3) pregnancy associated α_1 -glycoprotein (SP₂) and 4) pregnancy associated α_2 -glycoprotein (SP₃). HPL and SP₁ appear only during pregnancy and are considered pregnancy specific, but SP₂ and SP₃ are present in minute volumes in the serum of non-pregnant women and in males. Moreover, as they show marked increases with pregnancy, they were called "pregnancy associated proteins". Subsequent study revealed that SP₃, that is pregnancy associated α_2 -glycoprotein

(α_2 -PAG), was the protein, PZP, discovered by Smithies¹⁹).

Quantitation of α_2 -PAG can be done by 1) single immunodiffusion¹³), 2) Laurell's immunoelectrophoresis method²⁰), 3) radioimmunoassay⁸), 4) enzyme-immunoassay²¹), 5) solid-phase fluoroimmunoassay⁴) etc., and basic and clinical studies on it are being performed.

The clinical implications of α_2 -PAG have not been established, but many researchers have reported on its behaviour in a variety of diseases. MacLaren et al.¹²) have reported that this protein increases with the use of oral contraceptives. It is also reported to be increased in serum of patients with Behçet's disease²⁴) and rheumatoid arthritis^{11,19}). There are also reports that it is increased in patients with malignancies such as breast cancer^{16,21}), ovarian cancer¹⁷), choriocarcinoma⁵), gastric cancer¹⁵), urinary bladder cancer¹⁵) and malignant melanoma^{1,15}). α_2 -PAG has become one of the many tumor markers, and much attention is now being focussed upon it.

On the other hand, reports on its behaviour in renal diseases are rare. In 1972, Horne et al.⁹) determined the α_2 -PAG concentration in 53 patients with renal diseases, and reported that the level was significantly higher in patients with proteinuria than in those without it. In 1983, we reported that the level was higher than healthy subjects in patients undergoing chronic hemodialysis²⁶) and those with nephrotic syndrome²⁷), and also noted that there was a correlation with the clinical activity in the latter. However, no reviews have been made of the relationship between the serum α_2 -PAG level and histological type of glomerulonephritis. Thus, we made a study of the α_2 -PAG behaviour in IgA nephropathy patients. The results showed the level in IgA nephropathy patients was increased as compared with healthy subjects. Also in male patients the level was significantly higher in those with proteinuria in comparison with those without it, and further there was a negative correlation between renal function. Care must be exercised in the interpretation of these results, but as there are reports that α_2 -PAG has some sort of immunosuppressive substance^{10,23,25}), we presume α_2 -PAG is involved in some form in the development of IgA nephropathy which is induced by abnormalities in the immune system. Further,

it is considered possible that the determination of serum α_2 -PAG may be useful in assuming the prognosis of IgA nephropathy. However, there are yet many unknown aspects of α_2 -PAG such as in what organ it is produced and its role. Thus, it is considered further study is required.

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