

# URINARY FIBRIN (-OGEN) DEGRADATION PRODUCTS IN RUSSELL'S VIPER (*DABOIA RUSSELLII SIAMENSIS*) BITE VICTIMS

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**Abstract.** Serum and urine concentrations of fibrin (-ogen) degradation products (FDP) were estimated in 20 proven Russell's viper bite (RVB) cases with severe defibrination. All patients had similar degrees of high serum FDP levels. However, the ten who developed into acute renal failure (ARF) had significantly ( $p < 0.001$ ) higher urinary FDP levels than those who did not. The urinary FDP levels of ARF cases increased correspondingly with high serum FDP levels but not in cases without ARF. Serial comparison of serum and urinary FDP levels in RVB cases with severe defibrination may be of value in predicting the likelihood of developing ARF. The present study favored disseminated intravascular coagulation as the main cause of ARF in Myanmar RVB cases.

## INTRODUCTION

In Russell's viper (*Daboia russelii siamensis*) bite, acute renal failure (ARF) is known to be one of the serious, common complications and it is not prevented by monospecific antsnake venom (ASV) therapy even when given within 4 hours of bite (Myint Lwin *et al.*, 1985). According to the report of Hla Mon *et al.* (1981), the commonest cause of ARF among patients admitted to Yangon General Hospital (YGH) was Russell's viper bite (RVB), with a mortality of 35%. Although many studies regarding ARF following RVB have been done, the pathogenesis of ARF in RVB is very complex and is still controversial.

Than Than *et al.* (1987) showed that serial monitoring of serum fibrin (-ogen) degradation product (FDP) levels was of value in predicting impending complete defibrination. The present study was done to determine whether the serial estimation of urinary FDP level could be of diagnostic value in predicting the development of ARF in the management of RVB.

## MATERIALS AND METHODS

The study was carried out at the Thayarwady Township Hospital about 130 km north of Yangon, during the rice harvesting season (November-January) of 1987-88. Twenty cases of confirmed RVB were included in the study. Confirmation of

RVB was done by identifying the dead snake brought to the hospital or by detecting specific venom antigen level in the patient's serum (Tun Pe *et al.*, 1991). All of these patients had incoagulable blood indicating systemic envenomation with severe defibrination. Although ten patients who did not develop ARF were treated with either 40 ml or 80 ml of ASV (Myanma Pharmaceutical Industry), all of those with ARF had received 80 ml.

The blood for estimation of FDP was collected through a 18-gauge plastic cannula into a FDP tube containing thrombin and soy bean trypsin inhibitor (Thrombo Wellcotest). Urine samples were also collected in FDP tubes at the time of venepuncture. Both blood and urine samples were taken before the administration of ASV and then repeated at regular intervals thereafter. These samples were incubated at 37°C for 30 minutes and then centrifuged at 3,000 rpm for 15 minutes. The serum and supernatant urine samples were collected in new tubes which were stored at -20°C for a week prior to transportation to the Department of Medical Research (DMR). In DMR these samples were stored at -80°C until tested.

Venom antigen in blood samples was detected by enzyme immunoassay (EIA) (Tun Pe *et al.*, 1991). FDP was measured by using Thrombo Wellcotest latex agglutination test kit (Wellcome Diagnostics).

The statistical significance for the difference

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between the urinary FDP levels in cases with and without ARF was tested by using the median test (Siegal, 1956).

### RESULTS

Out of 20 cases included in the study, ten patients went into oliguric renal failure (urine output < 400 ml/24 hours) and were transferred to Renal Medical Unit, Yangon General Hospital for further treatment. Peritoneal dialysis was done in five patients who recovered later. Of the remaining five patients, in whom peritoneal dialysis was not done, three patients expired and the other two recovered with conservative treatment.

The maximum serum venom antigen levels of patients with ARF (range 60-100 ng/ml, median 75 ng/ml) and those without ARF (range 50-90 ng/ml, median 80 ng/ml) were more or less the same. However, the interval between the time of bite and the administration of ASV was longer in patients without ARF (range 0145-1535 hours, median 0723 hours) than in patients with ARF (range 0050-0910 hours, median 0225 hours).

Fig 1 shows the serum FDP levels of patients with and without ARF. As all of these patients had severe disseminated intravascular coagulation (DIC), their serum FDP levels were very high and they directly corresponded to the venom antigen levels (Fig 2).

Fig 3 illustrates the urinary FDP levels of both groups. The urinary FDP levels of cases with ARF were significantly ( $p < 0.001$ ) higher than the cases without ARF. Besides, the urinary FDP levels of ARF were correspondingly increased with serum FDP level. However in the latter group, apart from the urinary FDP levels of three patients at 6 hours and only one patient at 12 hours after ASV were > 160  $\mu\text{g}/\text{ml}$ , the serial urinary FDP levels were mostly between 10 and 80  $\mu\text{g}/\text{ml}$ .

### DISCUSSION

Our study firstly showed that in RVB cases with severe defibrination, the serial comparison of serum and urinary FDP levels could be useful for predicting the development of ARF. Thus, patients who had high urinary and serum FDP levels later

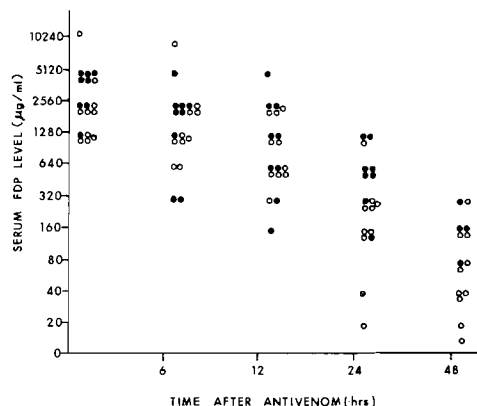


Fig 1—Serum FDP levels of Russell's viper bite victims with (●) and without renal failure (○).

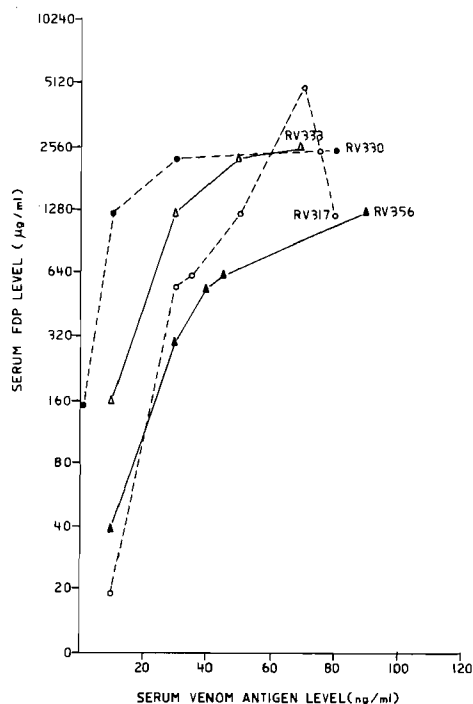


Fig 2—Relationship between serum FDP and serum venom antigen levels in Russell's viper bite victims with ( $\Delta$ — $\Delta$ ) and without renal failure ( $\circ$ -- $\circ$ ).

developed ARF, but those who had high serum with comparably low urinary FDP levels did not do so.

In patients in whom DIC occurred, the presence of FDP in serum was directly related to the extent of fibrin deposition and the preceding fibrinoly-

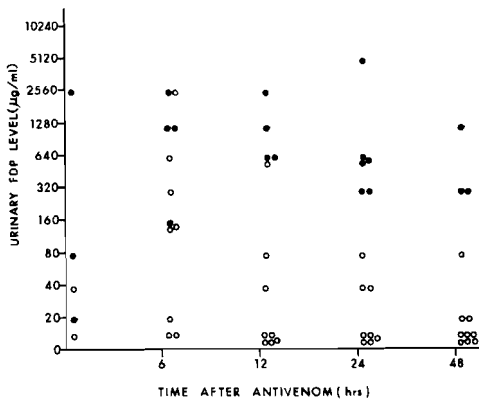


Fig 3—Urinary FDP levels of Russell's viper bite victims with (●) and without renal failure (○).

tic activity. As the reticuloendothelial system takes part in the clearing of serum FDP (Stiehm *et al.*, 1971), the urinary FDP level of our patients may partly reflect the amount of intraglomerular fibrin deposition and local fibrinolytic activity as occurs in glomerulonephritis. Therefore, it is suggested that the increased intraglomerular fibrin deposition occurred more markedly in our ARF cases. Aung Khin (1978) also found intraglomerular fibrin deposition in both experimentally Russell's viper envenomated animals and in human RVB victims by light microscopy and electron microscopy. Hence, the main possible cause of ARF in our patients was intraglomerular fibrin deposition rather than a direct nephrotoxic action of the venom, as evidenced by higher urinary FDP levels than in the control group.

A question arose from the study about the cause of increased intraglomerular fibrin deposition in RVB cases with ARF, as both groups had almost the same venom antigen levels and the same degree of DIC. This might be a consequence of anaphylactic reaction such as occurs with increased TPA-1 in RVB cases (Woodhams *et al.*, 1988).

The present study indicated that, once the severe DIC set in, the development of ARF did not depend either on the amount or the time (*ie* how early it is given) of ASV treatment. This finding is contrary to those of others (Matthai and Date, 1981; Jeyarajah, 1984) who suggested that the early antivenom treatment within 2 to 5 hours of the bite might prevent renal failure. This may be true before the blood has severely defibrinated but once this has occurred there will be deposition

of microthrombi in the microcirculation of various organs, mainly the kidneys. This contributes to the lowering of glomerular filtration rate and irreversible acute tubular necrosis which in turn causes acute renal failure.

Therefore, the finding of a high urinary FDP level, indicating increased intraglomerular fibrin deposition, favors DIC as the main cause of ARF and supports the suggestion of Woodhams *et al.*, (1988) for using recombinant TPA to activate fibrinolysis. Furthermore, progression of RVB cases (with severe defibrination and high serum/urinary FDP levels) to ARF suggested the value of serial comparison of serum and urinary FDP levels in predicting impending ARF in these cases.

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