

**To Study the Role of Forced Alkaline Diuresis in Prevention of Acute Kidney Injury in Patients with Hematotoxic Snake Bite****Guruprasad Shetty<sup>1</sup>, Mrunalini TR<sup>2</sup>, Shreedevi Yenni<sup>3</sup>, Varun Byrappa<sup>4</sup>**<sup>1</sup>Assistant Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Kaher, Belagavi<sup>2</sup>Senior Resident, Department of Emergency Medicine, Kempegowda Institute of Medical Sciences, Bangalore<sup>3</sup>Associate Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Kaher, Belagavi<sup>4</sup>Associate Professor, Department of Emergency Medicine, Kempegowda Institute of Medical Sciences, Bangalore

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Conflict of interest: Nil

**Abstract:**

**Background:** Snake bite is a common medical emergency and an occupational hazard, more so in tropical India, where farming is a major source of employment. Viper bites are more common than other poisonous snakebites in humans. INDIA is among the countries most dramatically affected by snake bite and accounts for almost half the total number of annual deaths across the world. According to WHO estimate- India had 1.2 million snake bite deaths from 2000-2019 and nearly half of the victims aged 30-69 and over a quarter being children under 15. The WHO has set the target of reducing these deaths to half the number by 2030 and India's efforts to prevent and control these deaths will largely influence this global target. To avoid gross under reporting, few authors have even recommended Government of India to designate and enforce snake bite as "NOTIFIABLE DISEASE" within Integrated Disease.

Surveillance Program. More than 2700 species of snakes exist in the world, of which only 450 have front fangs making them capable of injecting venom during bite. India harbors more than 250 species and subspecies, out of which around 50 are venomous. Hence the need for a useful tool to fight the most dreaded complication of snake bite is necessary.

**Methods:** After obtaining approval and clearance from the institutional ethics committee, a study was conducted in the department of emergency medicine in KIMS over a period of 1.5yrs which included 25 patients above the age of 18 years. Each patient with a definitive history of snake bite was admitted, evaluated and considered for forced alkaline diuresis based on the relevant comorbidities. Patient was followed up throughout the stay and renal functions monitored. Patients who failed were taken up for hemodialysis and outcome of the procedure charted.

**Results:** In the study, 20% were <30 years, 40% were 31 to 40 years, 28% were 41 to 50 years, 12% were >50 years. 36% were Female and 64% were Male. At baseline 24% had metabolic acidosis and 76% had Normal ABG. In the study, HB was  $12.97 \pm 2.25$ , TLC was  $11271.6 \pm 4019.09$ , Platelets was  $2.33 \pm 0.99$ , Neutrophil was  $81.94 \pm 9.63$ , Lymphocyte was  $18.05 \pm 9.81$ , Monocyte was  $4.68 \pm 5.35$ , Basophil was  $0.88 \pm 2.13$  and Eosinophil was  $1.44 \pm 2.74$ . In Fang Marks Distribution, 4% had in Left Ankle, 28% had in Left Foot, 4% had in Left Great Toe, 12% had in Left Hand, 4% had in Left Thumb, 4% had in Left Wrist, 8% had in Right Ankle, 8% had in Right Finger, 4% had in Right Foot, 12% had in Right Hand, 8% had in Right Leg and 4% had in Right Toe. Most common site of fang marks was Left Hand and Right Hand (12% respectively). In 2D echo, 8% had LVH and 92% were WNL. In Doppler, 60.0% had No DVT and for 40% doppler was not done. Cellulitis was present in 64%. Cycle 1 FAD was Done in 100.0%, 24.0% in cycle 2, 8.0% in cycle 3. Haemodialysis was done in 4% of subjects.

**Interpretation & Conclusion:** Forced alkaline diuresis proved to be a good intervention to save patients from developing or worsening AKI. It is a much-needed tool in our country which contributes significantly to snake bite related deaths. It also helps to decide on early intervention with hemodialysis, in case of failure to respond to FAD.

**Keywords:** hematotoxic snake bite, forced alkaline diuresis, acute kidney injury, hemodialysis.

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## Introduction

Snakebite is an acute life threatening, time limiting medical emergency, and an occupational hazard, more so in tropical India -amongst farmers, plantation workers, and other outdoor workers and results in much morbidity and mortality throughout the world.

The involvement of the predominantly young, healthy and the working population in rural areas which are compounded by poverty and the lack of access to health care services in these areas, signify the social and economic impact of this problem[1].

As snakes are natural habitats of rural areas, more than 97% snakebites happen in the rural areas. Incidence of Snakebite depends on frequency of contact between snakes and human. Snakes are usually elusive and reclusive. [1,3]

Snakebites occur when human move to the habitat of snakes like paddy field, tea, rubber and coffee plantations, bushes for open field latrine, and besides the water bodies during fishing. Bites may be inflicted at home by peri-domestic species which lives in roof space or under floor. Seasonal peak of snakebite is noted in summer and rainy seasons. Increase in agricultural activity or heavy rain leading to flooding of the natural habitats of snakes increase the chance of snake human contact. During flood there may be epidemic of snakebite.[3] Walking bare foot either in dark or in undergrowth increases chance of snakebite. Bites occur with Common Kraits when they come to homes for prey or probably by attraction of human sweat, and when someone sleeping on floor rolls over the snake.

In recent years, few cases of Snakebite and fatality were recorded in unscientific and casual handlers or venomous snakes by snake rescuers and snake charmers.[3]

The World Health Organization has estimated that nearly 1,25,000 deaths occur among 2,50,000 poisonous snake bites worldwide every year, of which India accounts for 10,000 deaths [4,5].

More than 2700 species of snakes exist in the world, of which only 450 have front fangs making them capable of injecting venom during bite.

Clinical effects of envenomation by same species of snake are almost similar except a few regional variations. Kraits are active during night hours, often biting a person sleeping on floor bed. Maximum Viper and Cobra bites occur during the day or early darkness, while watering the plantation or walking bare foot in grown grass or soybean crops. [6] India harbors more than 250 species and subspecies out of which around 50 are venomous. Only 5 venomous species pose a threat to public health in India. [1,2] ICMR finds only 30% of snake bite victims in Rural India reach hospitals. ICMR is the apex body in

India for the formulation, coordination and promotion of biomedical research and has released a study-protocol on the incidence, mortality, morbidity and socioeconomic burden of snake bites.[7, 10]

Snake bites kill more than 46,000 people in india every year. Most victims in rural india are more dependent on alternative methods which are not recorded in national registries [7]

A study, Million Death Study (MDS) undertaken by Registrar General Of India (RGI), is implemented in close collaboration with the Centre for Global Health Research at the University of Toronto, leading Indian and overseas institutions, and ICMR. RGI-MDS conducted the first snakebite study in India and focused prospectively on the incidence of snake bites in 5 regions of India and 13 States with population of 84 million (covering 6.12% of total population of our country). The study duration is for 18 months from April 2022 to October 2023.

Around 46,900 people die due to venomous snake bites in India annually. Only 20-30% of snake bite victims seek treatment in hospitals, the study has suggested.

Geographically, the greatest impact of snakebite is in the tropical and subtropical regions, with the highest occurrence in India. Global estimates of snakebite range from 4.5 million to 5.4 million bites annually with an estimated 2 million of them in India with significant physical, mental and socioeconomic consequences[9]

## Methodology and Materials

A prospective study was started after obtaining clearance from the Ethical Committee at KIMS, Bangalore. Study was conducted from February 2021 to october 2022. Subjects were included based on Inclusion and exclusion criteria-

### Inclusion criteria

- Subjects above the age of 18 yrs.
- Subjects with definitive history of Viper snake bite.

### Exclusion criteria

- Age less than 18 years.
- Subjects who are not willing or have not consented for the study.
- Known case of past renal disease or ultra-sonographic evidence of bilateral small kidneys or patients with baseline creatinine of >1.5mg or any previous medical records.
- Known case of diabetes or hypertension.

**Statistics**

**Sample Size**

Sample size was estimated by using the proportion of AKI after forced alkaline diuresis at 0.5% from the study by Pratik giri et al. using the formula

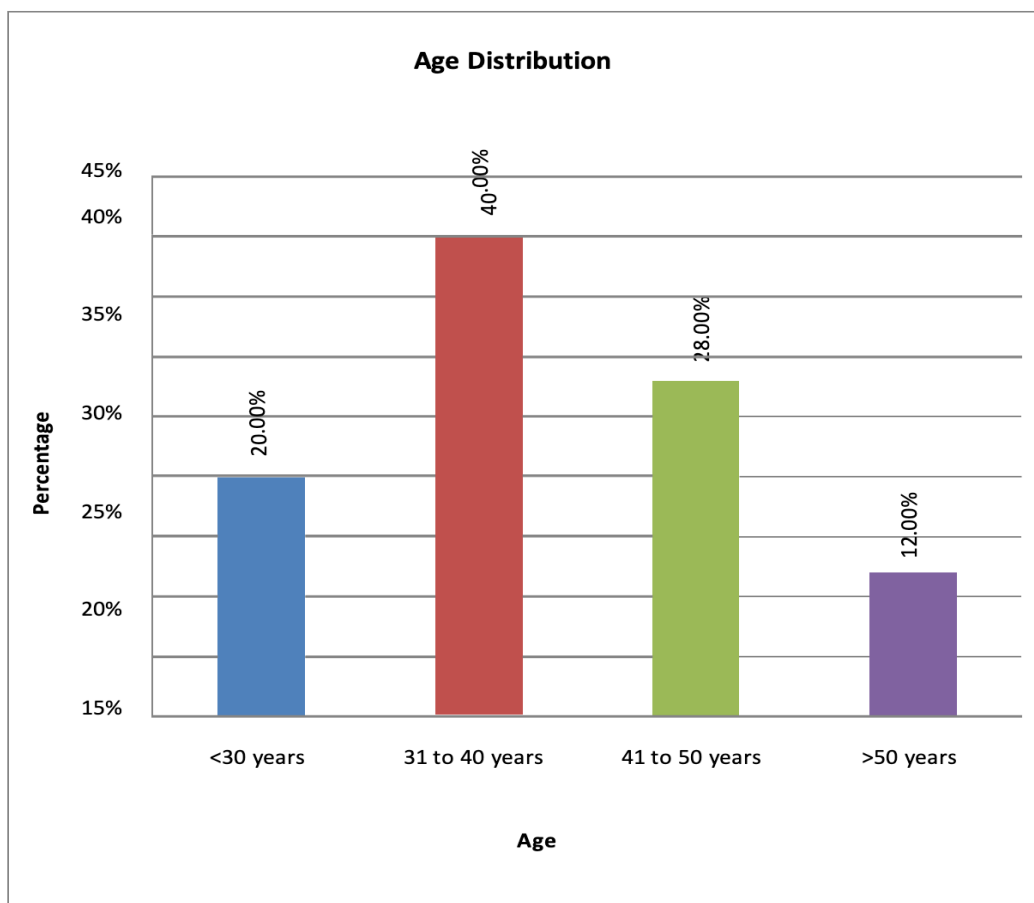
**Results**

25 subjects, fulfilling the inclusion criteria were thoroughly studied and results were charted as follows.

**Table 1: Age distribution**

		Count	%
Age	18-30 years	5	20.0%
	31 to 40 years	10	40.0%
	41 to 50 years	7	28.0%
	>50 years	3	12.0%
	Total	25	100.0%

In our study, 20% were between 18-30 years, 40% were 31 to 40 years, 28% were 41 to 50 years, 12% were >50 years.



**Figure 1: Bar Diagram Showing Age distribution.**

**Table 2: Gender distribution**

		Count	Column N %
Gender	Female	9	36.0%
	Male	16	64.0%
	Total	25	100.0%

In our study, male preponderance of 64% was seen, females were 36%.

Gender Distribution

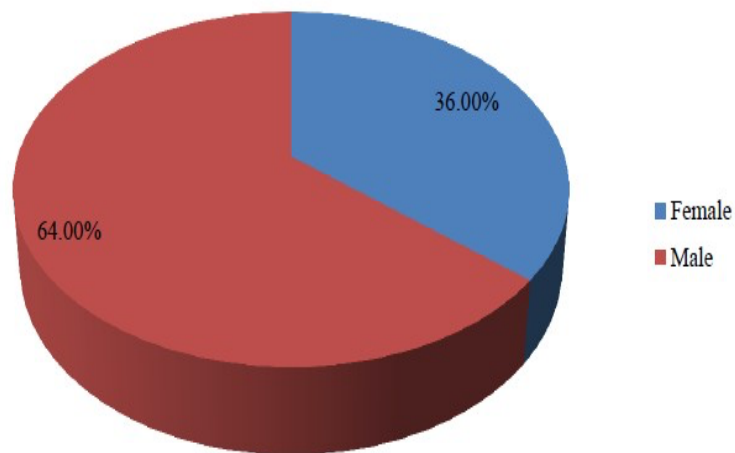


Figure 2: Pie Diagram Showing Gender Distribution

Table 3: Vital parameters at baseline

	Mean	SD	Median
SBP	135.52	26.57	130
DBP	84.56	15.65	80
PR	94.68	19.27	90
SPO2	96.48	2.14	96.00%
GRBS	168.60	61.42	170

In our study, SBP was  $135.52 \pm 26.57$ , DBP was  $84.56 \pm 15.65$ , PR was  $94.68 \pm 19.27$ , SPO2 was  $96.48 \pm 2.14$  and GRBS was  $168.6 \pm 61.42$ .

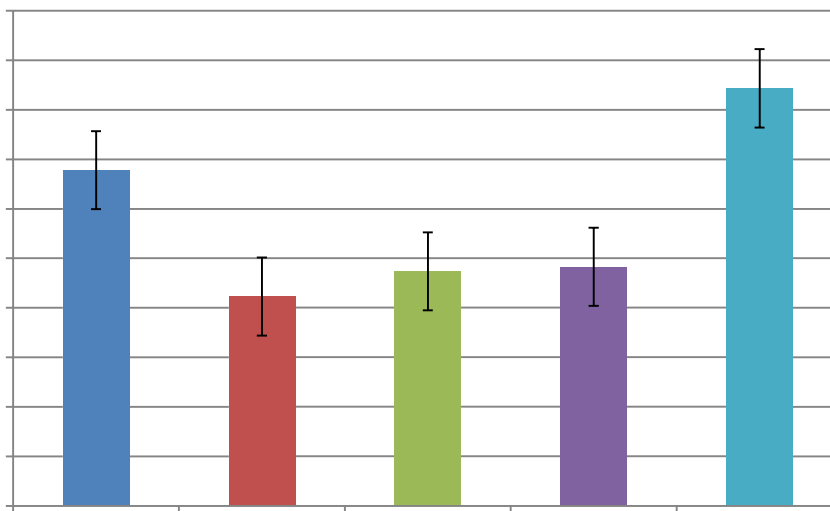


Figure 3: Bar Diagram Showing Vital parameters at baseline

Table 4: WBCT at baseline

WBCT	Count	%
>20	25	100.0%

At baseline WBCT was >20 in 100%. Of snake bite victims.

Table 5: ABG at baseline

ABG	Count	%
MA-C	6	24.0%
WNL	19	76.0%

In the study, at baseline 24% and had metabolic acidosis and 76% had Normal ABG.

ABG at baseline Distribution

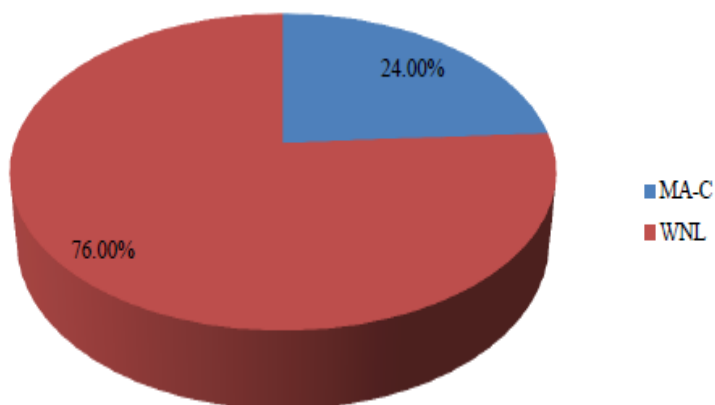


Figure 4: Pie Diagram Showing ABG at baseline

Table 6: CBC at baseline

	Mean	SD	Median
Hb	12.97	2.25	12.80
TLC	11271.60	4019.09	10990
Platelets	2.33	0.99	2.28
Neutrophil	81.94	9.63	80.0
Lymphocyte	18.05	9.81	20.00
Monocyte	4.68	5.35	3
Basophil	0.88	2.13	0
Eosinophil	1.44	2.74	0

In the study, HB was  $12.97 \pm 2.25$ , TLC was  $11271.6 \pm 4019.09$ , Platelets was  $2.33 \pm 0.99$ , Neutrophil was  $81.94 \pm 9.63$ , Lymphocyte was  $18.05 \pm 9.81$ , Monocyte was  $4.68 \pm 5.35$ , Basophil was  $0.88 \pm 2.13$  and Eosinophil was  $1.44 \pm 2.74$ .

CBC at baseline

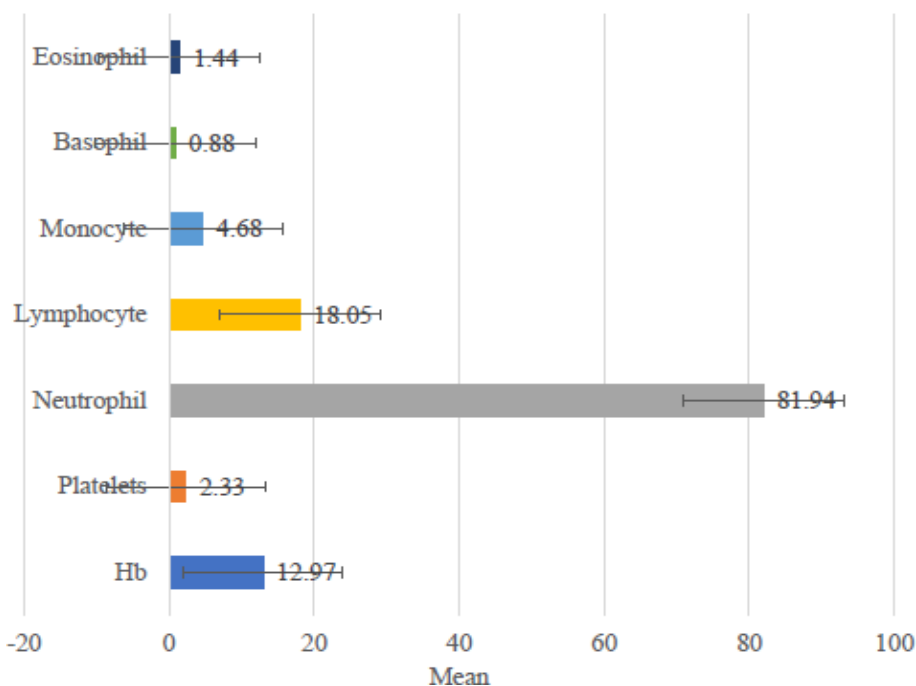


Figure 5: Mean CBC at baseline distribution

## Discussion

A prospective study was done with sample size of 25 subjects with proven Viper snake bite who presented to KIMS, Bangalore between February 2021 and October 2022, after obtaining Ethical Committee clearance.

Our study included a total of 9 female patients and 16 male patients.

Subjects who satisfied the inclusion and exclusion criteria were included in the study.

In our study, 20% of the subject were 18-30 years, 40% were 31-40 years, 28% were 41-50 years and 12% were >50 yrs.

Time since bite in majority was >10 hrs (32%), followed by 2 to 4 hrs (28%) and 4 to 6 hrs (28%).

- Local swelling at the site of bite.
- Bleeding from the bite sites.
- Black or brown urine. The black or brown urine which was positive for RBC or Hb.
- Time in between snakebite and administration of anti-snake venom.
- Twenty minutes whole blood clotting time (20 min WBCT).
- CPK levels.
- Total amount of anti-snake venom given. ASV was given to the snakebite patients with one or more of the following criteria:
  - 20 min WBCT > 20 min.
  - Presence of cellulitis
  - Spontaneous bleeding from the bite site or any other site.

After explaining the procedure (forced alkaline diuresis) and its complications, written consent was taken.

Vitals parameters at the baseline were within normal limits-SBP was  $135.52 \pm 26.57$ , DBP was  $84.56 \pm 15.65$ , PR was  $94.68 \pm 19.27$ , SPO2 was  $96.48 \pm 2.14$  and GRBS was  $168.6 \pm 61.42$ .

After primary survey and initial assessment of the patient, treatment as per Standard Treatment Guidelines were started along with forced alkaline diuresis followed by dyselectrolytes (mostly, hypokalemia) corrections.

25 patients were given- 10 vials ASV stat followed by 3 vials TID till 30 vials of ASV is completed according to Standard Treatment Guidelines-isotonic crystalloids up to 20ml/kg/hr to maintain urine output of 2-3ml/kg/hr, analgesics (NSAIDs was not used), antibiotics, correction of dyselectrolytes (hypokalemia was anticipated and corrected with 20meq of KCL in maintenance fluid after each cycle of FAD). One patient was given 40 vials of ASV

because of worsening cellulitis. Two patients were given 20 vials because they showed no overwhelming signs of systemic envenomation.

All the subjects had a WBCT of >20 minutes. At baseline 24% had metabolic acidosis and 76% had Normal ABG. This was essential to rule out impending renal failure and early need for hemodialysis.

In the study, HB was  $12.97 \pm 2.25$ , TLC was  $11271.6 \pm 4019.09$ , Platelets was  $2.33 \pm 0.99$ , Neutrophil was  $81.94 \pm 9.63$ , Lymphocyte was  $18.05 \pm 9.81$ , Monocyte was  $4.68 \pm 5.35$ , Basophil was  $0.88 \pm 2.13$  and Eosinophil was  $1.44 \pm 2.74$ .

In 2D echo, 8% had LVH and 92% were WNL.

In Doppler, 60.0% had No DVT and for 40% doppler was not done as there was no evidence of cellulitis or local swelling.

In Cycle 1 FAD was Done in 100.0%, 24.0% in cycle 2, 8.0% in cycle 3.

Urea levels at Baseline was  $34.64 \pm 15.971$ , at Cycle 1 was  $25.52 \pm 8.799$ , at Cycle 2 was  $30.5 \pm 21.8701$  and at Cycle 3 was  $59 \pm 22.627$ .

There was a significant decrease in Urea levels after Forced Alkaline diuresis among all patients after cycle 1. (p value = 0.001)

Creatinine levels at Baseline was  $1.244 \pm 0.69407$ , Cycle 1 was  $1.048 \pm 0.5221$ , Cycle 2 was  $1.517 \pm 1.0759$  and Cycle 3 was  $2.6 \pm 0.2828$ .

There was a significant decrease in Creatinine levels after Forced Alkaline diuresis among all patients after cycle 1. (p value= 0.012)

Prateik giri et al studied a total of 50 students presenting to ED with vasculotoxic snake bite their study noticed that 26 patients i.e. about 52% of the total were asymptomatic who did not require any treatment except observation for 24 hours. Rest 24 patients developed some symptoms of snake envenomation. Out of these, a total of 8 patients who are falling in the inclusion criteria for the study had received forced alkaline diuresis 2 or 3 cycles; and it is found that none of the patients who received forced alkaline diuresis developed acute kidney injury shown by rise in serum creatinine level or decreased urine output.

## Result

Prevalence of acute kidney injury in snake bite patient is 20 %, which was shown by rise in serum creatinine level and decreased urine output. The prevalence of AKI in patients who received forced alkaline diuresis as treatment modality along with anti-snake venom is 0%.

Similarly in our study Forced Alkaline Diuresis was an effective tool to reduce the possibility of worsening or developing AKI secondary to snake bite provided patient presented to the Tertiary care early.

5 patients out of 25 underwent second cycle of FAD too, due to persistent AKI. 2 out of those 5 patients underwent third cycle of FAD and one patient underwent Hemodialysis after the third cycle because of worsening AKI. That patient underwent dialysis because FAD could not prevent AKI and she developed features of volume overload and oliguria (0.5ml/kg for 6 hours of urine output). This condition can likely be attributed to late presentation to hospital, but more studies are needed to prove this.

### Conclusion

Hence, our study concludes that AKI due to hemotoxic snake bite is a correctable red flag sign and Forced Alkaline Diuresis is an effective tool for the same. As this is life threatening, effective measures can help curb the mortality and morbidity if patients present early.

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