



ROLE OF NYCOCARD D-DIMER TEST IN PREVENTION OF THROMBOTIC CATASTROPHES IN ASYMPTOMATIC HEALTHY INDIVIDUALS SERVING AT HIGH ALTITUDE

Ajay Dheer*

Sikkim Manipal Institute of Medical Sciences, Sikkim, India *Corresponding Author

VK Mehta

Sikkim Manipal Institute of Medical Sciences, Sikkim, India

ABSTRACT The personnel serving in high altitude environment are at definite risk in suffering catastrophic thromboembolic events due to being in hypercoagulable state for prolonged periods. The various presentations of thrombosis include deep vein thrombosis (DVT), pulmonary thrombo-embolism (PTE), portal/splenic vein thrombosis, cerebral venous thrombosis, etc. Early diagnosis of thrombosis minimizes the risk of thrombo-embolic complications, reduces the morbidity, mortality and averts the exposure of patients without thrombosis to the risks of anticoagulant therapy. There are no tools presently available to screen populations staying in high altitude with possible high risk of such complications. **D-dimer test** is considered as one of the possible tests for such screening. The D-dimer test by NycoCard D-dimer Single test on NycoCard Reader II was selected based on its high sensitivity of detecting D-dimer and being routinely used in the military hospital. Moreover, it could be conveniently done in a field setting. The tests were conducted in situ as per the procedure by trained lab technician.

KEYWORDS : High altitude area, thromboembolism, D-dimer Test

The personnel serving in high altitude environment specially those in the armed forces are at definite risk in suffering catastrophic thromboembolic events due to being in hypercoagulable state for prolonged periods. Several physiological adaptation i.e., rise in red blood cell counts and increase in haemoglobin concentration (to maintain oxygen transport in the hypobaric environment), increased platelet count, platelet activation take place in the body. Further, raised fibrinogen level combined with hypoxia and dehydration cause a thrombotic milieu to occur, leading to thrombosis in normal individuals.(1,2) **It is evident that there is a definite rise of thrombotic events in individuals staying at higher altitudes.(3,4)**

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D-dimer is a unique degradation product produced by plasmin mediated proteolysis of cross-linked fibrin. D-dimer test being quite sensitive, is of immense value to diagnose DVT and resultant PTE.(5) The negative predictive value (NPV) of this test is excellent as it can easily rule out PTE.(6) The problem is high frequency of false positive results with D-dimer in certain conditions. While recognizing the good NPV but poor positive predictive value (PPV) in clinical settings, D-dimer test was carried out on a population serving in high altitude environment, who are known to have high incidence rates of thrombotic events.(7)

In this study, we evaluated the usefulness of the **NycoCard D-dimer test** in identifying those asymptomatic healthy soldiers serving at high altitude, who may go on to suffer a thrombotic catastrophe. It may help prioritize speedy evacuation from peripherally located posts and prevent such catastrophe. **The comparison of rates of incidence of thrombotic catastrophe between D-dimer positive and D-dimer negative individuals are measured, for whom other risk factors such as age, gender, altitude of stay, duration of stay at high altitude etc., are same.**

Materials and Methods

The study was conducted in a high altitude terrain in Himalayan Mountain ranges of East Sikkim wherein soldiers are staying at

altitudes between 2400m – 5400m. Healthy soldiers having stayed between 3600m – 4500m (II Stage) for a minimum of eight weeks continuously and those having stayed between 4500m – 5400m (III Stage) for a minimum of six weeks continuously were randomly enrolled. They were tested for D-dimer values in situ by **NycoCard D-dimer Single test on NycoCard Reader II**. These individuals were closely monitored for an end result i.e. a thrombotic event, at their respective locations for three months.

All methods of estimating D-dimer may not be equally sensitive or specific. However, keeping in view the procedure and convenience to conduct in situ, D-dimer was tested by **NycoCard D-dimer Single test on NycoCard Reader II**, which is based upon an immunometric flow-through principle and can be performed easily in field conditions. Plasma samples were prepared from whole blood with sodium citrate as anticoagulant. After separation of plasma by centrifugation, specimens were tested. D-dimer level of **>0.3 mg/L** was considered to be positive and these individuals were kept under close surveillance/monitoring at their respective locations. The primary outcome was considered as a thrombotic event viz., DVT, cerebrovascular accident, cerebral venous sinus thrombosis, PTE etc., which occurred within three months.

Individuals with recent hospitalization (02 weeks), acute febrile illness, known liver disease, cardiac disease, history of recent surgery (within 04 weeks), recent poly trauma (within 04 weeks), past history of stroke, venous thromboembolic events were excluded from the study.

Results

171 healthy soldiers aged between 20 years to 50 years (**Mean 33.82 ± SD 7.17**). The participants belonged to six different geographical parts of the country. Of the participants, 137 (80%) were located between 3600m - 4500m (II Stage) while 34 (20%) were located between 4500m – 5400m (III Stage). The duration of stay of the participants (**Mean 15.46 weeks ± SD=5.75 weeks**) was as per the protocol. The haemoglobin (**Mean 16.39gm/dL ± SD=0.89 gm/dL**), was almost 2 gm/dL higher than that at lower altitudes, indicating that the participants had attained adequate physiological adaptation in high altitude.

D-dimer value higher than the cut-off of 0.3 mg/L (range 0.8 - 0.4 mg/L) was found in 24 participants. The relationship between D-dimer positive/negative value and occurrence of any thrombotic event during three months of follow-up was closely monitored. It was observed that no participant in either D-dimer positive or D-dimer negative group developed any thrombo-embolic event. In the absence of the primary outcome during the study period, the sensitivity and specificity of the test as a tool for prevention of thrombotic catastrophe could not be commented upon.

The result of D-dimer test is given at Table 1.

Table 1 : Result of D-Dimer Test 7

Total	D-Dimer test		% + ve
	-ve	+ve	
171	147	24	14

Discussion

There are several studies that have shown a higher risk of thrombotic events in such populations who serve for long duration at high altitudes. Anand et al reported a 30 times higher risk of spontaneous vascular thrombosis on long term stay at high altitude in Indian soldiers. Veins are common sites for such thrombotic events. Jha et al reported that long term stay at high altitude with polycythemia vera and hypercoagulable states were associated with high risk of stroke. (8,9,10,11)

D-dimer test is a sensitive and a positive test which indicates the presence of an abnormally high level of fibrin degradation products in the body. It indicates that there has been significant clot (thrombus) formation and breakdown in the body. However, false positive results are also seen in other conditions such as pregnancy, infection, malignancy etc. **The specificity of this test is considered to be on the higher side in the individuals posted at high altitude since they have attained a hypercoagulable stage due to normal physiological adaptation.**(12)

In our study the high values of the D-dimer test, however, did not predict the occurrence of a thrombotic event in a three month follow-up period of healthy subjects. The study carried out in hospitalised patients of suspected pulmonary thrombo-embolism, suggest the importance of a positive D-dimer test in prioritizing evacuation of symptomatic patients from remote high altitude areas to hospitals.(12) In our study 24 asymptomatic individuals who tested positive did not develop any thrombotic disease during the follow up period of three months. Hence, the test cannot be used as a screening tool for prevention of a thrombotic event at high altitudes.

Conclusion

In our study, the role of D-dimer test by NycoCard Reader II, in prevention of thrombotic catastrophe, in asymptomatic healthy individuals staying at high altitude i.e. its utility in predicting the occurrence of a thrombotic disease has not been established. **Although, there is evidence that significant level of D-dimer is present in 14% of our subjects staying in high altitude, but that has not resulted in a thrombotic catastrophe.** Therefore, a separate study e.g. marker-based, may be required to study the peculiarity of a thromboembolic phenomenon, with an aim to prevent such catastrophic illnesses in high altitude.

There has been no study conducted or any test identified so far to **prevent Thrombotic Catastrophes in asymptomatic healthy soldiers serving at High Altitude.** This study is therefore a pioneering effort.

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