**Abstract**

Results obtained using multifactorial stress model (air-exposure, submergence, hypoxia) showed that elevation of RBC, HB, Ht and blood glucose was linearly correlated with progressive stress uniformly. Submergence caused rapid stress with blood glucose reaching 50% elevation within 60 min. Hypoxic water with access to air had very little effect on blood glucose. Similarly, lowering the temperature significantly affected the blood parameters. The air-exposure model was also used for testing lysozyme activity and phagocytosis assay during stress. Plasma lysozyme was significantly lower in air stressed fish. Submergence increased the number of granulocyte, lymphocytes and activity of phagocytic cells. Spleen and kidney lysozyme activity increased significantly. The titer of total non-specific immunological increased during submergence. But no such effect was observed in air-exposure. These results suggest that submergence stress in stimulating non-specific defense system in the air-breathing fish, *Osphronemus olfax*. This is the first report that submergence stress is playing the role of an immunomodulator in an air-breathing fish