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Role of Tumor Necrosis Factor-alpha in Pediatric Tuberculosis

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Abstract: The study was conducted on, 15 normal control (group I) and 30 children with tuberculosis (group II). Both groups were subjected to full medical history, careful clinical examination and laboratory investigations that included ESR, CRP, tuberculin test and sputum culture. Chest X-ray was also done. Serum level of TNF-α was done by ELISA technique. The mean value of TNF-α 51.6 (± 34.7) pg/ml was higher in patients than controls 9.5 (± 1.4) pg/ml with high statistical difference. There was a statistically significant difference between serum level of TNF-α and ESR, CRP and radiological findings of chest. No statistically significant difference was found between TNF-α and tuberculin test or sputum culture. It is concluded that elevated serum level of TNF-α in tuberculosis is important to antimycobacterial immune defenses although excessive TNF-α may be associated with tissue damage.

Key words: TNF-α, tuberculosis, children, ELISA

Introduction

Tuberculosis continues to be a major threat to health throughout the world (Kochi, 1991). In developing countries, tuberculosis still constitutes a major health problem with high prevalence of both infection and disease (Donia, 1981). Understanding the immunological mechanisms of protection and pathogenesis in tuberculosis remains problematic (Flyan *et al.*, 1995). Mycobacterial tuberculosis was a strong inducer of Tumor Necrosis factor-alpha (TNF-α) in human monocytes (Averill *et al.*, 1995). TNF-α one of the cytokines contributes both to protection against tuberculosis and to immunopathology (Flesch and Kaulmann, 1993 and Flyan *et al.*, 1995).

The aim of present work was to assess the serum level of TNF-α in tuberculosis and its relation to laboratory diagnosis of tuberculosis.

Materials and Methods

This study included 45 children attending El-Galaa-Teaching Hospital and Giza Chest Hospital from January to July 2001.

The children were divided into following groups:

Group I: Control group of 15 normal children, 7 males and 8 females. Their mean age was 8.5 years.

Group II: Tuberculous group, including 30, with pulmonary tuberculosis (15 males and 15 females). Their mean age was 7-8 years.

Both groups were subjected to full medical history and careful clinical examination. Routine urine and stool examination were done to exclude parasitic infestation. E.S.R. by Westergren method (Dacie and Lewis, 1984) and CPR by latex agglutination slide test supplied by SAS scientific USA (Mackie and McCarney, 1995) were performed. Tuberculin test (Mackie and McCarney, 1995) and Sputum culture by Zeil Nelseen (ZN) staining were studied, with radiological examination of chest for both groups together with assessment of Serum level of TNF-α by ELISA technique supplied by Genzme USA (Mackie and McCary, 1995). Statistical analysis of data was performed by an IBM personal computer using the program microstat.

Results

In Table 1 the mean serum level of TNF-α in tuberculous group was 51.6 (± 43.9) pg/ml which was higher than its level in control group 9.5 (± 1.9) pg/ml and this difference was highly significant.

In Table 2 the mean value of serum level of TNF-α and laboratory diagnostic tests in tuberculous group showed that there was a statistically significant difference between TNF-α and ESR and CRP while no significant difference was observed between TNF-α and tuberculin test or sputum culture.

In Table 3 the mean serum level of TNF-α in patients with + ve chest radiological findings was higher than its level in patients with –ve chest radiological findings.

Table 1: The mean value of serum level of TNF-α in both studied groups.

	TNF-α (pg/ml)			
Studied groups	No. of cases	Range	Mean (± SD)	P value
1. Group I control group	15	7-15	9.5 (± 1.9)	< 0.005 highly sign.
2. Group II Tuberculous group	30	5-200	51.6 (± 43.7)	

There was highly significant difference between both study groups as regards the serum level TNF-α.

Table 2: The mean value of serum level of TNF-α and diagnostic laboratory tests in tuberculous group

		TNF-α (pg/ml)			
Diagnostic lab. tests		No. of cases	Range	Mean (± SD)	P value
(1) E.S.R	+ ve	25	10-200	51.2(± 40.5)	< 0.05 Significant
	-ve	5	5-70	32.3(± 11.3)	
(2) CRP	+ ve	27	10-200	52.1(± 49.5)	< 0.05 Significant
	-ve	3	5-10	6.6(± 1.5)	
(3) Tuberculin	+ ve	9	10-80	35.7(± 25.6)	> 0.05 Significant
	-ve	21	5-200	58.1(± 46.9)	
(4) Sputum culture	+ ve	18	5-200	57.9(± 48.6)	> 0.05 Significant
	-ve	12		42.9(± 32.7)	

There was highly significant difference between TNF-α and ESR, CRP while, there was no significant difference between TNF-α and tuberculin test and sputum culture.

Discussion

Tuberculosis is still a medical problem in many countries including Egypt. Over the past decade understanding of the pathophysiology of systemic inflammatory response has advanced considerably with the improved understanding of cytokines and its effect (Law *et al.,* 1996). The role of TNF-α in tuberculosis may be beneficial (protective) or deleterious (pathological) (Otsuka *et al.,* 1990).

The T-cell mediated response would lead to the production of inferferon-Y which cause local activation of macrophage (Rook *et al.,* 1986). Those activated macrophages have an enhanced capacity for TNF-α production (Barnes *et al.,* 1994). TNF-α enhances the chemotaxis of macrophages and increases their phagocytic activation (Djeu *et al.,* 1988). In the same time circulating TNF-α inhibits neutrophil migration to local inflammatory sites, a result that might indicate an inhibitory role of TNF-α (Kaplan, 1994).

The mean serum level of TNF-α in the tuberculosis group was higher than in the control group and this difference was statistically significant (P< 0.005) Table 1.

Table 3: The mean value of serum level of TNF-α and radiological findings of chest in tuberculous group.

Diagnostic	TNF-α (pg/ml)			
lab. tests	No. of cases	Range	Mean (± SD)	P value
+ ve	7	30.200	95(152.7)	< 0.0005
-ve	23	5-110	36.5(+ 26.1)	Highly signif.

There was a highly significant difference between TNF-α and radiological findings of chest in tuberculosis.

This result is in agreement with Akalin *et al.* (1994) and Foley *et al.* (1993) who found that patients with tuberculosis exhibited statistically significant elevation of TNF-α level as compared with the control group.

Also serum level of TNF-α was higher in tuberculous cases with elevated ESR and + ve CRP results than tuberculous cases with normal ESR and CRP. The difference was statistically significant (P< 0.0005) (Table 2). This may be explained by the fact that TNF-α induces hepatocytes – mediated acute phase (Oppenheim *et al.,* 1991).

On the other hand the mean value of TNF-α in patients with + ve tuberculin test and sputum culture and those with –ve tiuberculin test and sputum culture showed no statistically significant difference (P> 0.05) (Table 2).

In contrast to these results, Ogawa *et al.* (1991) found higher serum level of TNF-α in patients with positive tuberculin test than those with –ve tuberculin test. This difference in results can be explained by the effect of other factors like corticosteroid therapy, severity of tuberculosis or nutritional status.

The mean value of TNF-α in patients with radiological chest signs was higher than in those with no radiological signs and the difference was highly statistically significant (P< 0.0005) (Table 3). These results are in accord with those of Hirano *et al.* (1990) who reported that excessive local production of TNF-α may cause marked lung damage. Kim *et al.* (1991) also reported that patients with moderate to far advanced infiltration of their chest X-ray showed a significantly higher level of serum TNF-α than those with normal involvement.

We conclude that tuberculous patients have a higher level of TNF-α and it has + ve correlation with ESR, CRP and + ve radiological chest signs. Other studies to assess value of TNF-α in follow up of tuberculous cases and its level in different forms of tuberculosis and various forms of treatment are recommended.

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