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# The Assessment of IL-12+P40 among Primary pulmonary and Chronic (Old) Pulmonary Tuberculosis

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## Abstract

*The possible role of Il-12 +P40 assessment as a biomarker for tuberculosis disease is being reported. It was found thatIL-12+p40 can discriminate between PPTB, sputum AFB shedders OPTB and sputum non AFB shedders as concentration means are taken in consideration . Since there were a range of individual variations in tuberculosis patients and controls, reflecting variations in genetic backgrounds of the best control groups. All of the aforementioned forms of tuberculus disease in man rises up the levels of IL-12+P40 . Such IL-12+P40 level rising in OPTB was diseases stage and patients age dependent. Conversely, inhibition occurred in Il-12+P40 levels with chronicity at the age ranges of 25-34y and 40-55y. Sputum AFB shedders in OPTB group associated with high IL-12 +P40 levels, while, the non shedders were with low IL-12+P40 levels . In PPTB group, however, there were with neither age range dependence nor inhibition of IL-12+P40 level could be noted.*

**Keywords**: Il-12 +P40, biomarker, tuberculosis.

## Introduction

Tuberculosis as an infectious diseases in man is rather common nationally[1] and internationally[2]. It is interesting since it affects many people all over the world and it is a model diseases for intracellular bacterial pathogen breaching natural humoral and cellular immune factors as well as inducing Th1 and Th2 responses[3-5]. Th1 response, however, is protective diagnostic and paralleled with delayed type hypersensitivity[3]. The Mycobacterium tuberculosis epitopes induces monocytes, dendertic cells, B lymphocytes, T helper 1 and T helper 2 cytokines[3,4]. Several workers have been tried to putdown disease classification in accordance with cytokines profiles of different immune cells involved in tuberculosis[4-9] . In the present work we tried to use IL-12 p40 as biomarker for delineating primary from old pulmonary tuberculosis.

## Material and Methods

Forty – six tuberculus patients were diagnosed (table-1)[2]. They were selected for determination of IL-12+P40 in patient sera using ELISA technique in accordance with manual procedure of BioSource[10]. ESR determinations were made as in Deice and Lewis[11].

## Results and Discussion

The controls (C). the old, chronic tuberculosis (OPTB), the overall and the primary pulmonary tuberculosis (PPTB) were showing IL-12P40 concentration means of 224 pg/ml, 232.34 pg/ml , 395.4 pg/ml and 475.95 pg/ml respectively . Both of the disease forms were of higher concentration means than the control, but, OPTB group was slightly higher than the C. group, as showing in figure-1.

**Table-1**
**Tuberculus patients Characteristics***

| No. | Character | PPTB. | OPTB. |
|---|---|---|---|
| 1. | Patient No. | 24 ! | 22 ! |
| 2. | Age group | | |
| | 15-19 | 2 | 1 |
| | 20-24 | 4 | 3 |
| | 25-29 | 2 | 4 |
| | 30-34 | 3 | 3 |
| | 35-39 | 2 | 3 |
| | 40-44 | 4 | 1 |
| | 45-49 | 2 | 3 |
| | 50-54 | 2 | 2 |
| | >55 | 2 | 2 |
| 3. | Signs and symptoms | | |
| | Sweating | ++ | +/- |
| | Temp. | + | + |
| | Loss of weight | ++ | + |
| | Difficult breathing | ++ | ++ |
| | Cough | ++/B | + |
| | ESR | H. | M. |
| | AFB | +/- | +/- |
| | Skin DTH | +/- | +/- |
| | Chest X ray | + | ++/- |

(*) Grange [12,13]. ! = Total No. of patients. PPTB.= Primary pulmonary Tuberculosis, OPTB= Old pulmonary Tuberculosis. B. = Bloody.

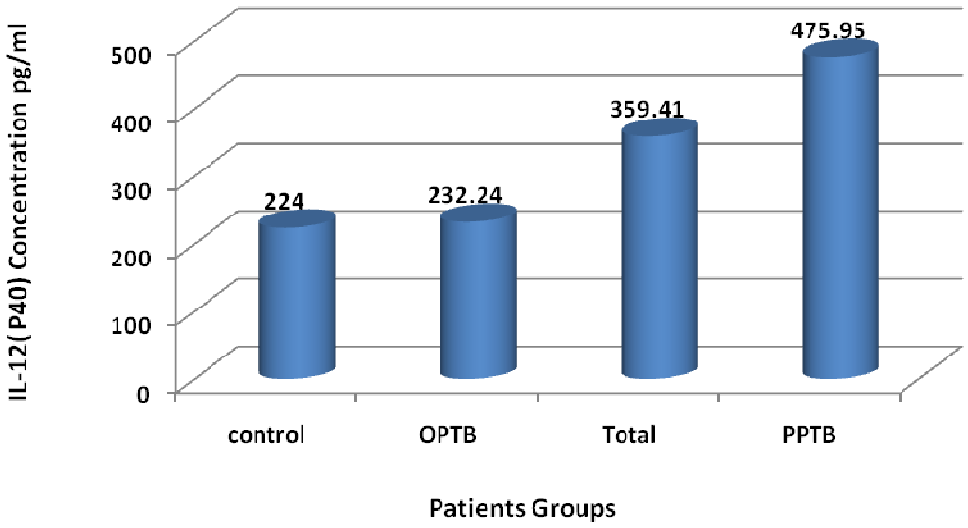


**Figure - 1**
**IL-12 40 levels in various tuberculosis disease forms**

All age ranges of PPTB were with concentration means of IL-12P40 approximate two fold the control value, while OPTB were showing age dependent variation such as the age range 15 -24 y, it was around two folds, while in the age range 35 -39 y it reaches around 1.5 folds the C. group. Other age range were showing 120 -218 pg/ml as shown in table 2. At the age range of >55 years the IL-12P40 levels were 124 and 524 pg/ml for OPTB and PPTB respectively. Aging alone in PPTB group doesn't affect IL-12P40 concentration, while aging and chronicity in OPTB group affect decrease in IL-12P40 concentrations. However , chronicity in the age range of 15-24 y mediate increase of up to 500 -515pg/ml in OPTB and being higher than those of PPTB at same age ranges which were ranging between 314 -461 pg/ml as in table -2.

**Table -2**
**IL-12P40 concentration means in relation to age ranges of tuberculus patients.**

| No. | Age range | IL-12P40 pg/ml | |
|---|---|---|---|
| | | PPTB | OPTB |
| 1. | 15 -19 | 314.6 | 515 |
| 2. | 20 -24 | 461 | 500 |
| 3. | 25-29 | 611 | 144 |
| 4. | 30 -34 | 647.6 | 120 |
| 5. | 35 -39 | 495.5 | 362 |
| 6. | 40 -44 | 476 | 38 |
| 7. | 45 -49 | 526 | 115 |
| 8. | 50 -54 | 236 | 218 |
| 9. | > 55 | 529 | 124 |

The OPTB sputum AFB shedders were of higher IL-12P40 concentration means than those OPTB sputum AFB non shedders showing in table-3.

**Table-3**
**IL-12+P40 in relation to sputum AFB shadings in OPTB group**

| Groups | Shedders | Non shedders |
|---|---|---|
| **Patient numbers** | 7 | 15 |
| **% of Total** | 31.8 | 68.18 |
| **IL-12 P40 Value** | 341.28 | 201.86 |

The normal distribution of IL-12P40 values for each individual in patients and control groups were showing notable degrees of variations as showing in figure-2.

The patterns of IL-12P40 levels that parallels ESR and age range were being as IL-12P40 increase there were ESR increase and the higher IL-12P40 values patients were the higher ESR values in PPTB group . while there was no such association can be made in OPTB group as showing in table-4.

**Discussion:** Human interleukin -12 p40 were assessed in the sera of primary, old AFB shady and non shades pulmonary tuberculosis tables 1-4. IL-12 is a 75 KDa lymphokines produced mainly by monocytes, macrophages, B- lymphocytes and dendertic cells. Il-12 shows an unusual heterodimeric structure composed of one 40 KDa (P40) and of one 35KDa (P35) subunits linked together by disulphide bonds. P35 sub unit is distantly related to IL-6 and G-CSF while P40 shows homology to the extracellular domain of the alpha chain of Il-6 receptor. This suggests that IL-12 may have evolved from a cytokine/ soluble receptor complex. P40 is secreted in large excess over the biologically active heterodimer. P40 is in receptor binding but P35 is necessary for signal transduction. Monomers and mainly homodimers of P40 show antagonist activity to IL-12[10].

IL -12 can discriminate between the different studied forms of human tuberculosis as showing in figure - 1. This finding was in agreement with Sutherland et al using combination of IL-12P40 , IL-17 and TNF alpha leading to increasing in correct tuberculosis classification of majority of cases[8] .

IL-12P40 in this study were showing variable concentration among the different study PPTB and OPTB patients such finding has been noted by De Jong et al[14] working on African tuberculosis.

Anti TB. Treatment for two months has been shown to increase in IL-12 P40 by monocytes[15]. In comparison this study figure-1 was showing decrease of IL-12P40 on therapy and chronicity.

In general, youth state is associated with potent activities of the immune system as apparent in young tuberculosis patients IL-12 P40 values (figure-1, tables (-2,-3 ). While aging are mostly associated with decline in the immune system activities , this , together with disease chronicity were leading to decrease in levels of IL-12 P40 concentration means as showing in tables (-3 and -4)[16].

Individual variations noted in figure - 2 may reflects the extent of variation in the genetic background of patients which might indicated the genetic heterogeneity of the patients[4].

In active chronic old TB patients, there were continual shedding of AFB in their sputum. This means continual bacterial induction to monocytes to produce IL-12P40[16-18]. In PPTB, ESR and IL-12P40 were high in levels. This means that in active primary diagnosed non treated PPTB, high inflammatory process parallels high IL-12P40 production by monocytes[15].

**Table-4**
**The patterns of ESR in relation to IL-12 P40 concentrations in tuberculus patients**

| No. | Age | PPT.B. | | | OPT.B. | | |
|---|---|---|---|---|---|---|---|
| | | No. | IL-12 | ESR | No. | IL-12 | ESR |
| 1. | 15 -19 | 3 | 315 | 80 | 1 | 515 | 30 |
| 2. | 20 -24 | 4 | 461 | 94 | 3 | 500 | 33 |
| 3. | 25-29 | 2 | 611 | 100 | 4 | 144 | 37 |
| 4. | 30 -34 | 3 | *644* | *90* | 3 | 120 | *35* |
| 5. | 35 -39 | 2 | 495 | 97 | 3 | 362 | 30 |
| 6. | 40 -44 | 4 | 476 | 92 | 1 | 38 | 20 |
| 7. | 45 -49 | 2 | 526 | 85 | 3 | 115 | 31 |
| 8. | 50 -54 | 2 | 236 | 82 | 2 | 218 | 25 |
| 9. | > 55 | 2 | 529 | 75 | 2 | 124 | 27 |

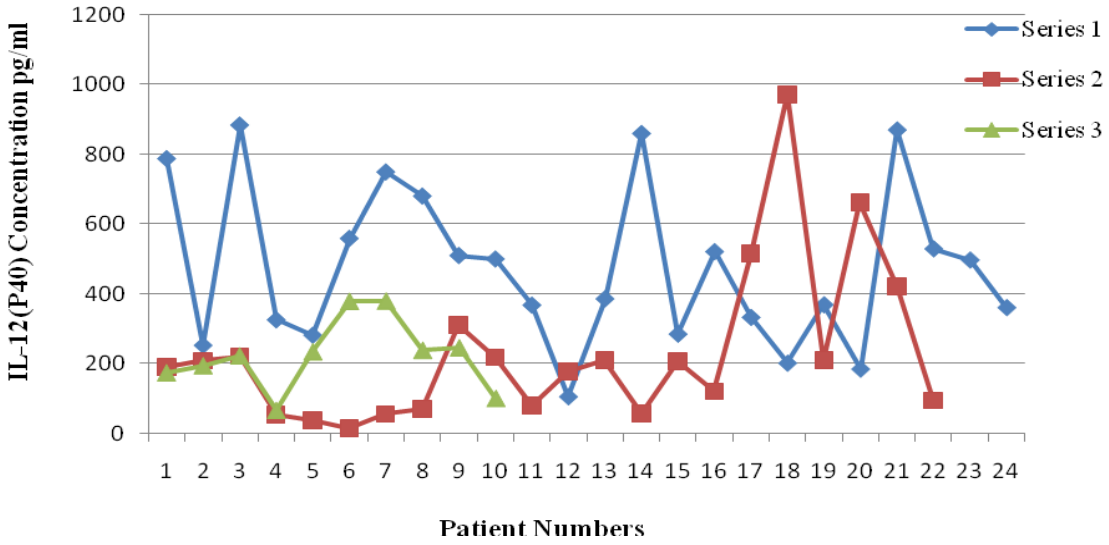


**Figure – 2**
**The normal distribution of IL-12 P40 among tuberculus patient and controls reflecting the extent of individual variations . (Series 1= PPTB. Series 2= OPTB. Series 3= control group)**

## Conclusion

The IL-12+P40 assessment in tuberculus patient can be useful as biomarker for disease delineation between primary, old shedder and old non shedder pulmonary tuberculosis.

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