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Isra University

IMPACT OF ISONIAZID AND/OR RIFAMPICIN ON CHEMOKINES AND CLINICAL PARAMETERS LEVEL IN TUBERCULOSIS PATIENTS

Prepared by

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A Thesis

Submitted to Faculty of Pharmacy as a Partial Fulfillment of the Requirement for Master Degree in Pharmaceutical Science

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DEDICATION

*I present this article to the great man my father (*ENG . AHMAED ODEH*) who support me in every time and the beautiful lady my mother and my special friend my brother and to my sisters.*

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LIST OF ABBREVIATIONS

NUMBER	Symbols	
1	7TM	7 transmembrane
2	ALP	Alkaline phosphatase
3	ALT	Alanine aminotransferase
4	AST	Aspartate aminotransferase
5	ATB	Active pulmonary tuberculosis
6	AUC	Area under the curve
7	BCG	Bacillus Calmette–Guérin
8	BLT1	leukotriene B4 receptor 1
9	BUN	Blood Urea Nitrogen
10	CAR	CXCL12 abundant reticular
11	CB2	cannabinoid receptor 2
12	CDC	Centers for Disease Control and Prevention
13	CMI	Cell mediated immunity
14	CTL	Cytotoxic CD8+ T lymphocytes
15	CYSLT1	Cysteinyl leukotriene receptor 1
16	DC	Dendritic cell
17	DM	Diabetes mellitus
18	EMA	European Medicines Agency
19	EMB	Ethambutol
20	EPTB	Extrapulmonary tuberculosis
21	FDA	Food and Drug Administration
22	G-CSF	Granulocyte-colony stimulating factor
23	GDP	Guanosine diphosphate

24	GIT	gastrointestinal tract
25	GPCRs	G-protein coupled receptors
26	GPI	Glycosylphosphatidylinositol
27	GRKs	G protein-coupled receptor kinases
28	GTP	Guanosine triphosphate
29	GUTB	Genitourinary tuberculosis
30	HIV	Immunodeficiency Virus Human
31	IFN-γ	interferon-γ
32	INH	Isoniazid
33	iNOS2	Inducible nitric oxide synthase
34	JAK-STAT	Janus kinase-signal transducer and activator of transcription
35	LAM	Lipoarabinomannan
36	LNTB	Lymph node tuberculosis
37	LTα	lymphotoxin α
38	MAC	Macrophages
39	MDR-TB	Multidrug-resistant tuberculosis
40	MO	Monocytes
41	Mtb	Mycobacterium tuberculosis
42	NKC	Natural killer cells
43	NKT	Natural killer T
44	NO	Nitric oxide
45	NRAMP1	Natural resistance-associated macrophage protein 1
46	PNG	Polymorphonuclear granulocytes
47	PPD	Purified protein derivative
48	PUO	Pyrexia of unknown origin

49	PZA	Pyrazinamide
50	RIF	Rifampicin
51	S1P1	Sphingosine-1-phosphate receptor 1
52	SM	Streptomycin
53	TB	Tuberculosis
54	TBM	Tuberculosis meningitis
55	TNF-α	tumor necrosis factor alpha
56	TST	Tuberculin skin test
57	VD	Volume of distribution

IMPACT OF ISONIAZID AND/OR RIFAMPICIN ON CHEMOKINES AND CLINICAL PARAMETERS LEVEL IN TUBERCULOSIS PATIENTS

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ABSTRACT

Tuberculosis (TB) is one of the most serious diseases that have been founded in ancient times and discovered even in the ancient Egyptian mummy. There are great challenges were faced by the medical staff like an early diagnosis and follow-up the improvement of patient's health. Assessment priorities of response to treatment regimen include both monitoring of treatment-induced adverse events, and estimation of biomarkers for treatment response in pulmonary and extra-pulmonary tuberculosis, which is important for the success of treatment.

Forty tuberculosis patients of pulmonary and extra-pulmonary were subjected to this study. Blood samples of TB patients were screened for serum biomarkers; Chemokine, Hematology; Hb, Monocytes, Lymphocytes, Neutrophils, WBCs, MCV, MCHC, MCH, PCV. Liver function tests; Aspartate aminotransferase, Alanine aminotransferase, Alkaline phosphatase, Bilirubin, Albumin. Kidney function tests; Creatinine, Urate, and Blood Urea Nitrogen, and the correlation between the parameters were measured for all. The monitoring and follow-up of all enrolled TB patients were assessed for the presence of any adverse effects, and the compliance/adherence to treatment by Isoniazid 300 mg/kg, and Rifampicin 600 mg/kg were recorded during the study period.

The results of this study showed that the percentage of pulmonary was 55%, and 45% of extra-pulmonary tuberculosis, total female to male percentage ratio was 42:58.

A significant difference was recorded between pulmonary and extra-pulmonary patients of the serum chemokine CXCL8 after one and two months of the treatment by Isoniazid and/or Rifampicin, the serum CXCL8 was increased in pulmonary and decreased in extra-pulmonary TB patients. Studies of the clinical parameters showed that the mean values of liver enzymes were very high in the pulmonary TB patients; AST and ALT were 90.22, 71.22, respectively. A significant difference was noticed in the levels of AST, and ALT between pulmonary and extra-pulmonary tuberculosis. Kidney function parameters showed a difference in creatinine level between the two studied groups.

Conclusion of this study described that chemokines play a role in mediating an effective immune-modulatory role during the treatment of TB infection, suggesting that such assessment may be useful for therapeutic efficacy of Mycobacterium tuberculosis infection and the therapeutic drug monitoring for the compliance to TB treatment. Also, the role of the pharmacist in the education of TB patients about their adherence to therapy to get maximum therapeutic efficacy and outcomes.