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SUPPLEMENTARY MATERIAL

A study of N-acetyltransferase 2 gene polymorphisms in the Indian population and its relationship with serum isoniazid concentrations in a cohort of tuberculosis patients

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Supplementary Table 1. Clinical data of tuberculosis patients as per their acetylator status.

Characteristics	Overall	Fast Acetylators (FA)	Intermediate Acetylators (IA)	Slow Acetylators (SA)
No. of patients, n	217	16	85	116
Sex, Male/Female	95/122	8/8	39/46	48/68
Age, years	25 (20-37)	24.5 (20.0-30.0)	26 (20.0-36.0)	25 (19.0-38.0)
Weight, Kgs	48 (41-55)	47 (42.25-54.25)	49 (41.5-55)	46 (40-55.25)
Type of TB				
Pulmonary, n	100	10	47	43
Extrapulmonary, n	117	06	38	73
Habitat				
Smoking, n	12	02	06	04
Alcohol, n	11	01	04	06
Comorbidities				
Diabetes Mellitus, n				
Yes	09	01	02	06
No	208	15	83	110
HIV, n				
Yes	08	00	03	05
No	209	16	82	111
Relapse of TB, n				
Yes	15	00	05	10
No	202	16	80	106
Family History of TB, n				
Yes	16	02	07	07
No	201	14	78	109
Adverse drug reactions (ADRs), n				
Yes	69	02	25	42
No	148	14	60	74
Gastrointestinal (GI) disturbances, n	19	02	06	11
Skin related, n	05	00	02	03
Eye related, n	02	00	01	01
Convulsion, n	01	00	00	01
Hepatotoxicity, n	42	00	16	26
Isoniazid (INH) dose, mg/kg	5.0 (4.33-5.59)	4.84 (4.39-5.58)	4.79 (4.41-5.44)	5.0 (4.24-5.63)
Serum Isoniazid concentration, 0hrs, µg/ml	2.6 (1.46-5.36)	2.13 (1.6-2.68)	2.14 (1.38-4.4)	3.54^{*} (1.49-6.17)
Serum Isoniazid concentration, 2hrs of drug intake, µg/ml	5.89 (4.06-8.55)	4.08 (3.47-5.15)	5.35 (3.69-7.41)	$7.02^{***\$\$}$ (4.69-9.85)

The continuous data are represented in Median and Interquartile range (IQR) and categorical data are represented as numbers. $^{*}p<0.05$; $^{***}p<0.001$ in comparison to FA and $^{\$\$}p<0.01$ in comparison to IA using Kruskal Wallis test followed by Dunn's multiple comparison post hoc test.

Supplementary Table 2. Allelic and genotypic frequencies of *NAT2* polymorphism in tuberculosis patients (n=217).

SNPs	Genotype Frequency n (%)
NAT2*5 481C>T (rs1799929)	
CC	94 (43.32)
CT	98 (45.16)
TT	25 (11.52)
Allele frequency	
C	0.66
T	0.34
Chi-square	0.005
p value	1.0
NAT2*6 590G>A (rs1799930)	
GG	101 (46.54)
GA	90 (41.47)
AA	26 (11.98)
Allele frequency	
G	0.67
A	0.33
Chi-square	0.73
p value	0.69
NAT2*7 857G>A (rs1799931)	
GG	185 (85.25)
GA	28 (12.90)
AA	04 (1.84)
Allele frequency	
G	0.92
A	0.08
Chi-square	5.00
p value	0.08

Supplementary Table 3. Allelic, genotype frequency and serum INH concentrations of *NAT2* acetylators in Indian tuberculosis patients (n=217).

NAT2 genotype	NAT2 genotype Frequency (n)	Acetylation status & Genotype Frequency (%)	Allelic frequency (%)	Median serum INH concentrations (µg/ml)	
				0 hours	**2hours**
NAT2*4/*4	16	7.37	Fast Acetylators (FA)-27.0 Slow Acetylators (SA)-73.0 HWE: χ2-0.006; p value-1.0	2.13 (1.60-2.68)	4.08 (3.47-5.15)
Total	**16**	**Fast Acetylators 7.37**		**2.13 (1.60-2.68)**	**4.08 (3.47-5.15)**
NAT2*4/*5	44	20.28		2.13 (1.49-4.98)	4.97 (3.57-7.04)
NAT2*4/*6	30	13.82		2.28 (1.09-4.17)	6.01 (5.15-8.63)
NAT2*4/*7	11	5.07		2.03 (1.55-3.52)	4.56 (4.13-7.03)
Total	**85**	**Intermediate Acetylators 39.17**		**2.14 (1.38-4.4)**	**5.35 (3.69-7.41)**
NAT2*5/*5	25	11.52		3.99 (2.02-6.26)	8.04 (5.47-9.77)
NAT2*6/*6	26	11.98		2.41 (1.38-5.20)	6.26 (5.05-8.03)
NAT2*7/*7	03	1.38		3.2 (2.20-3.50)	7.74 (6.22-8.15)
NAT2*5/*6	47	21.66		5.09 (1.75-7.09)	6.43 (3.79-10.80)
NAT2*5/*7	06	2.76		3.64 (1.33-6.24)	13.36 (9.40-18.38)
NAT2*6/*7	09	4.15		2.27 (1.25-2.60)	6.36 (5.53-10.17)
Total	**116**	**Slow Acetylators 53.46**		**3.54* (1.49-6.17)**	**7.02$^{***\$\$}$ (4.69-9.85)**

Serum INH concentrations are represented in Median and Interquartile range (IQR)
*p<0.05; ***p<0.001 in comparison to FA and $^{\$\$}$p<0.01 in comparison to IA using Kruskal Wallis test followed by Dunn's Multiple Comparison post hoc test

Supplementary Table 4. Relationship between *NAT2* acetylator and development of drug induced hepatoxicity and serum INH concentrations.

NAT2 acetylators	Crude OR	95% Confidence Interval (CI)	P value
NAT2 acetylator status and development of drug induced Hepatoxicity			
FA (Dominant Model) Reference (1.0)			
IA	7.83	0.48-137.48	0.068
SA	9.66	0.56-166.60	0.041
IA +SA	8.79	0.52-149.67	0.046
FA +IA (Recessive model) Reference (1.0)			
SA	1.53	0.77-3.06	0.23
NAT2 acetylator status and serum INH concentration at 2 hours post drug administration			
FA (Dominant Model) Reference (1.0)			
IA	0.96	0.19-4.82	1.0
SA	1.36	0.27-6.80	0.66
IA +SA	1.16	0.25-5.46	0.69
FA +IA (Recessive Model) Reference (1.0)			
SA	1.40	0.60-3.30	0.52

Data are represented as crude Odds Ratio (OR) and 95% CI. FA, fast acetylators; IA, intermediate acetylators; SA:, slow acetylators.