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PARTPEN T	CREENING OF HEALTHCARE AND NON- EALTH CARE WORKERS FOR PREVALENCE OF ATENT TUBERCULOSIS INFECTION AT ERTIARY CARE CENTRE, JAIPUR, RAJASTHAN	KEY WORD: latent tuberculosis infection (LTBI), Tuberculin skin test (TST), Healthcare workers(HCWs).		
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INTRODUCTION:-The Latent tuberculosis infection (LTBI) is described as "a state of a persistent immune reaction to stimulation by tubercular bacilli antigens without evidence of clinically manifested active TB". Approximately, 25% of the global population is infected with LTBI. Health-care workers (HCWs) are at high risk for acquisition of tuberculosis (TB) infection and disease than the general population because of their sustained occupational exposure to such infection. MATERIALS AND METHODS: A prospective study was carried out to assess the risk of TB infection among Healthcare workers and Non-healthcare workers. Risk assessment of latent TB infection done using single-step tuberculin skin test (TST) using 10 international units (IU; 0.1 ml) of tuberculin was done. TB infection was determined using a TST induration ≥of 10 mm as a cut-off point for TST positivity. The associations between TB infection and the sociodemographic characteristics, duration of possible exposure to TB, BCG scar, comorbidities were estimated using the Chi-square test. A two-sided P < 0.05 indicated statistical significance. RESULTS: A total of 135 eligible subjects consented to participate in the study. TST induration size and the TST results suggested that 36.29% (49/135) were infected with TB using a TST induration ≥10 mm as a cut-off point. Among 49 high risks, 27 resident doctors and 11 nursing staff were at high risks and 6 (12.2%) were non-healthcare workers. Statistical analysis suggested that age, duration of employment as a health-care professional, and working in medical wards/laboratories/offices were significantly associated with TB infection. CONCLUSION: The prevalence of LTBI is so high in countries like India that affected HCWs could not be exempted from working in high-risk areas. The situation is more perplexed in healthcare facilities with poor infection control measures. Another concern is even if found to have LTBI, there are no clear consensus guidelines about the treatment in high prevalence settings. So, implementation of proper safety control measures and increasing resources to adopt strategies to prevent and control TB in HCWs is of utmost importance.

INTRODUCTION:-

ABSTRACT

World Health Organization (WHO) declared Tuberculosis, a global health emergency for more than two decades now¹. Tuberculosis (TB) is a major cause of ill health and one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent. A combination of things including high costs, limited resources, and therefore the poor performance of varied diagnostic tests make the diagnosis of TB difficult in developing countries. Infection with Mycobacterium tuberculosis, in most individuals, is contained by the host immune defense mechanism and the infection remains latent. The Latent tuberculosis infection (LTBI) is described as "a state of persistent immune reaction to stimulation by tubercular bacilli antigens without evidence of clinically manifested active TB" ².Certain risk factors could potentiate the reactivation of LTBI, namely patients with HIV coinfection, hemodialysis, diabetes, immunosuppressive therapy, malignancy, organ transplantation, alcoholism, cigarette smoking, underweight, and malnutrition³⁻⁴. Healthcare workers (HCWs) are other victims with an increased risk of LTBI and TB disease, because of their sustained occupational exposure to such infection⁶. The situation is more perplexed in healthcare facilities with poor infection control measures. However, there remains a 10-15% lifetime risk of developing active TB. There is no gold standard test for the diagnosis of LTBI. The tuberculin diagnostic test is one among the few investigations dating from the 19th century that are still widely used as a crucial test for diagnosing tuberculosis infection. After such a long history, surprisingly, the interpretation of the test remains controversial.Various factors like age, immunological status, coexisting illness, etc. influence its outcome, so does its interpretation.

The WHO recommends three chemoprophylaxis treatment

options for LTBI, namely: six months of isoniazid (INH), three months of INH plus rifampicin (RMP), or a three-month regimen of weekly rifapentine plus INH.⁷ As there is a high incidence rate of TB in endemic areas without theavailability of routine LTBI screening for HCWs, the risk of TB reactivation and transmission is a potential threat.

Therefore, this study was deemed to be essential to assess the prevalence and associated risk factors of LTBI among HCWs, as well as to compare the prevalence among other working groupsandgeneral.

METHODS STUDY DESIGN AND SETTINGS

A prospective study was carried out at the Institute of Respiratory Diseases in a 1-year study period between April 2019 to March 2020 to assess the risk of latent tuberculosis infection among HCWs who are directly exposed to tuberculosis patients during medical duties. We also included non-healthcare workers who are not directly exposed to patients including office staff and some attendees of nontubercular patients who are not exposed to any known tuberculosis patients.

Among HCWs participants included resident doctors, nursing staff, laboratory technicians, and ward boys. All the HCWs who were engaged in medical duties for more than or equal to 6 months were eligible. The study was approved by the Ethics Committees of the Institute. 135 health-care workers, consented to participate in the study. This includes 52 resident doctors, 29 nurses, 7 laboratory technicians, and 9 housekeeping staff (Ward boys). Among the non-healthcare group of workers, 7 office staff and 31 attendants consented to participate in studies.

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DATA COLLECTION AND TUBERCULIN SKINTEST

All participants were interviewed about the assessment of TB infection among HCWs, including sociodemographic characteristics e.g., age, gender, contact history, years of exposure, BCG Scar, any comorbidities, knowledge of TB prevention and control, history of professional and clinical work.

A single-step TST using 10 international units (IU; 0.1 ml) of tuberculin (purified protein derivative) was performed. PPD-RT 23 with Tween 80 of strength 1 TU and 2 TU are standardized tuberculin available in India supplied by the Bacillus Calmette-Guerin (BCG) vaccine Laboratory, Guindy, Chennai. TST was administered using the Mantoux method and participants returned 48–72 h after TST inoculation to obtain results.

It is injected intradermally, using a tuberculin syringe 27 gauge from which 0.1 ml can be delivered accurately. A discrete, pale elevation of the skin (a wheal) 6 to 10 mm in diameter should be produced when the injection is given correctly. The test is given on the volar aspect of the left forearm to avoid errors in reading. However, the right arm may be used in case of any contraindicationto using the left arm.

The participants are instructed to keep the test site clean, and do not scratch or rub the area. The Mantoux skin test reading was done 48 and 72 h after administration in a good light, with the forearm slightly flexed at the elbow.

The horizontal diameter of induration size was measured using a standardized ruler, and the results were obtained after 72 hours. LTBI was determined using a TST induration \geq of 10 mm as a cut-off point for TST positivity. The basis of reading is the presence or absence of induration, which may be determined by inspection (from a side view against the light as well as by direct light) and by palpation. For standardization, the diameter of induration should be is recorded in millimetres (mm). The exact measurement of the induration in mm should be recorded. Erythema (redness) should not be measured.

Based on the size of induration we assigned them into three groups:-

 $\begin{array}{l} 0-5 \text{ mm} - \text{Group 1} \\ 6-9 \text{ mm} - \text{Group 2} \\ \geq 10 \text{ mm} - \text{Group 3} \end{array}$

Symptomatic individuals were further subjected to detailed clinical evaluation and radiological examination to rule out active TB. The associations between latent TB infection and the sociodemographic characteristics, duration of medical duties, BCG vaccination, any comorbidities, any side effects were estimated using the Chi-square test among different risk groups. A two-sided P < 0.05 indicated statistical significance.

RESULTS:-

The present study for the screening of prevalence of Latent tuberculosis infection (LTBI) in HCWs and Non-HCWs using Tuberculin skin test (TST) was conducted at the Institute of Respiratory Diseases, Jaipur. A total of 135 study subjects participated in our study. The age of the participants was between 20-60 years. Overall, the mean age of participants was 34.13 years. The mean age was 34.33 years in Group 3 (TST \geq 10mm) as shown in table 1. The mean duration of exposure was 6.28 years in Group 3 showing an association between increasing years of exposure to tuberculosis and developing LTBI as shown in table 2. The prevalence was 44.32% and 15.78% inHCWs and Non-HCWs, showing threefold higher risk in HCWs. Among HCWs, Residents (55.1%) are at higher risk of developing TB followed by nursing staff (22.4%) as shown in table 4. In Group 3, 43 study subjects out of 49 were HCWs and had LTBI. There was a significant association between the risk of developing active TB and

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occupation (Table 3). However, no significant association was seen between size of TST and sex, body mass index, comorbidities and BCG scar mark as shown in table 1.Mostly (79%) subjects were asymptomatic. 21% had symptoms in form of cough and fever.Few subjects had associated symptoms like loss of appetite and weight.

Table 1: Demographic characteristics and latent tuberculosis infection			
Factors		LTBI (%)	
Gender	Male	34/94 (36.17%)	
	Female	15/41 (36.58%)	
Mean Age		34.33 years	
BMI	>18.5	1/3 (33.33%)	
	18.5-25.0	45/121 (37.19%)	
	>25.0	3/10 (30%)	
BCG Scar	Yes	36/97 (37 11 %)	

Table 2:-Duration	of exposure (in years)	according to	risk
groups				

13/38 (34.21%)

4/11 (36.36%)

45/124 (36.29%)

No

Yes

No

Risk groups	Mean	Std. Deviation	Anova Test	p value
Group 1	1.09	2.05	6.29	0.002*
Group 2	3.56	3.66		
Group 3	6.28	8.24		
Total	4 23	5 89		

Table 3. Subgroup distribution according to risk groups

Subgroup		Risk groups			Total	Chi	p
		Group l	Group 2	Group 3		are	value
Attendants	N	11	14	6	31	31.7	<0.01*
	%	64.7%	20.3%	12.2%	23.0%	1	
Lab	Ν	0	5	2	7		
Technician	%	0.0%	7.2%	4.1%	5.2%		
Nursing	Ν	1	17	11	29		
Staff	%	5.9%	24.6%	22.4%	21.5%		
Office	N	2	5	0	7		
Workers	%	11.8%	7.2%	0.0%	5.2%		
Resident	Ν	3	22	27	52		
	%	17.6%	31.9%	55.1%	38.5%		
Ward Boy	Ν	0	6	3	9		
	%	0.0%	8.7%	6.1%	6.7%		
Total	N	17	69	49	135		
	%	100.0%	100.0%	100.0%	100.0%		

DISCUSSION:-

Comorbodities

In our study,overall 36.29% of study subjects(n=49) were infected with tuberculosis infection using TST induration \geq 10mm as a cut-off.In HCWs the prevalence was 44.32% and 15.78% in Non-HCWs showing three-fold higher risk in HCWs.This is in concordance with other studies.^{85,10,11,12,13}

This is likely due to high exposure to TB patients in the absence of optimum TB control measures in the high background TB prevalence in India in general and our study setting. In 2005, Pai et al.¹⁴ found the prevalence of 41% among HCWs.In 2010, Christopher et al.¹²estimated the prevalence to be 50.2%, with serial tuberculin testing.Studies from western countries like Canada and USA also reported LTBI prevalence higher in HCWs^{15,16.} Among healthcare workers resident doctors are found to be at higher risk. Resident doctors 27(55.1%), followed by nursing staff 11 (22.4%) are at high risk due to the long working hours and direct exposure to patients in hospital, making this group most vulnerable to LTBI. There is a two-fold higher risk of LTBI in medical residents as compared to nursing staff^{12,13,14} because during the phase of their training, a lot of importance is placed on bedside clinical work and they spend considerable time with patients, they are repeatedly exposed to patients with infectious TB during their ward duties.

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There is a significant association between years of exposure to tuberculosis and the prevalence of LTBI in the study population. The total mean duration of exposure was 4.23 years. The mean duration of exposure is 6.28 ± 8.24 in Group 3 and as low as 1.09 ± 2.05 in Group 1 in our study. In Group 2 it was 3.56 \pm 3.66. This relationship is significant according to our study. (P-value-0.002). Our study suggested that greater than five years spent in health care work in India is a strong risk factor for LTBI. Christopher et al¹² in their study showed that 76.6% of subjects had TST > 10mm after spending more than 5 years in healthcare work. Pai et al¹⁴ in their study in 2005 showed that 71% of participants with years of exposure more than 10 years are found to be TST positive with a cut of \geq 10 mm and participants with the duration of exposure >5 years and less than 10 years, 62 % found TST positive. Similar results were found in other studies ¹³ The mean duration of age was almost similar in all risk groups. No significant association was seen in our study.

A total of 41 (31.4%) females and 94 (69.6%) males participated in our study. Most studies conducted in India are female predominant, mainly due to the reason that they included nurses in their study in large number. Pai et al ¹⁴ in their study included 161 nurses, Christopher et al.¹² conducted their study among young nursing trainees, they included 412 females in their study. Jonagold et al.¹³included only 8 males in their study.

In Janagond et al ¹³ study, 37.5 % males and 32.3% females had an incidence of LTBI based on TST induration. Our study showed almost similar prevalence in both males and females. Most studies show male sex more vulnerable than females but no significant association was seen in any study.

BCG vaccination is given at birth as part of the national vaccination program in India. This explains the fact that most of the study participants had a vaccination scar. There is no significant correlation found in our studies between the presence of BCG scar and LTBI in the groups. 28.1 % of participants had no BCG scar. In Group 3 with TST \geq 10mm, BCG scar was not present in 26.5% study population. Janagond et al¹³ in their study also had similar results.

Other studies also showed similar results and no significant correlation was found in BCG vaccination and prevalence of LTBI.^{12,13,14,17}.Recent tuberculin surveys from India, involving more than 1,00,000 children, have also shown the BCG vaccination doesn't influence the estimation of the annual risk of infection.Our study correlated study subjects with comorbidities like systemic hypertension (HTN), diabetes, silicosis, chronic obstructive pulmonary diseases with no comorbid patients.No significant correlation was seen.

In our study no significant association of LTBI is seen with BMI. In other studies^{12,13,14} also, no significant relationship between BMI and LTBI was established. However, in our study 2 subjects with BMI 17.5 and 18.5 developed active TB during the course of study.

TST has evolved over 100 years; despite this, this test is still not devoid of side effects. Although adverse reactions to TST are uncommon, local allergic reactions to tuberculin or its components can occur in 2%–3% of those tested ¹⁸. Studies have side effects like itching, ulcer, blister formation, necrosis is in highly sensitive subjects. In our study, 26 (19.25%) subjects developed side effects. Local itching was the most common side effect in 24 subjects, one had an ulcer and one subject developed blister formation after the tuberculin test.

Further, all the symptomatic participants were subjected to detailed clinical and radiological evaluation in due course of our study. The two most common symptoms reported were fever and cough, few had associated symptoms like loss of appetite, loss of weight. They were subjected to radiological evaluation and further microbiological confirmation if suspected to have signs of active tuberculosis. 8 (8.24%) developed active tuberculosis during the study including 3 HCWs and 5 non-healthcare workers.

The TST is a simple test with low material costs that do not require a laboratory but do require a skilled person for testing. So, it has a role in detecting infection with M. tuberculosis. However further follow up to be done for these individuals and they should be evaluated and treated accordingly.

Limitations of our study:-

First, our sample size is small. Secondly, only one step TST was done. A negative test was not followed by another test to check booster phenomenon and testing at regular intervals not done to detect seroconversion.

CONCLUSION:-

Our study highlights, HCWs are at three-fold increased risk for acquiring LTBI than Non-HCWs. Mantoux test reactivity correlates with the medical duties performed like resident doctors and nursing staff is at higher risk of LTBI due to direct exposure to confirmed tuberculosis patients as compared to office workers and attendants. Similarly, duration of exposure is also significantly associated with Mantoux reactivity. So proper health measures must be emphasized like consistent N95 respirator use by HCWs while attending suspected or diagnosed TB patients. It is perhaps fair to conclude that, as of today, sparse evidence is available advocating the treatment of LTBI in HCWs irrespective of their contact with sputum smear-positive patients. Personal protective measures and close supervision are important to early diagnosis and prompt treatment.

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