# High Burden of Diabetes and Prediabetes among Adult Household Contacts of India

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## Background

- India has the largest burden of Tuberculosis (TB) and 2nd largest burden of diabetes and nearly 50% of diabetes goes undiagnosed.

- Diabetes and prediabetes increases and effective glycemic control decreases TB risk.

- While screening for TB among close contacts of TB, active screening for TB in diabetes and screening for diabetes in active TB is recommended by WHO and other guidelines, screening contacts for diabetes is not.

- There is scarce evidence on burden of diabetes or prediabetes among adult household contacts (HHC) of TB.

  We hypothesized high diabetes and prediabetes among adult HHC of TB patients because:

  - Diabetes is more prevalent among TB patients than the general population.

  - Both TB and DM are diseases linked to households due to shared genetics and shared lifestyle/environmental risks.

- Since HHC have a high prevalence of latent TB infections (LTBI) and TB disease, early diagnosis and management of diabetes among TB contacts could improve the prevention and treatment of TB as well as improve diabetes detection and care.

- We therefore assessed the prevalence of diabetes and prediabetes using systematic screening by glycosylated haemoglobin (HbA1c) among adult HHC of adult pulmonary TB patients in India.

## Methods

A cross-sectional analysis (at enrolment) of adult ($\geq$18 years) HHC of new adult pulmonary TB (PTB) patients enrolled in CTRIUMPh (Cohort for TB Research with Indo-US Medical partnership) study – an ongoing cohort of TB patients and their household contacts enrolled from August 2014 to May 2017 at NIRT, Chennai and BJGMC, Pune India.

- Key outcome variable: presence of diabetes and prediabetes. Irrespective of previously known diabetes, all contacts were tested for HBA1c.

- Those with known diabetes and HbA1c $\geq$6.5% were considered Diabetes and 5.7-6.4% were classified as pre-diabetes.

- Among diabetes, HbA1c $\geq$ 7% was considered to have 'poor glycaemic control'.

- Prevalence of diabetes and prediabetes was calculated, and we measured associations of diabetes with behavioural and clinical characteristics using prevalence ratio (PR) with 95% confidence intervals (CI).

- Factors with p-value <0.1 in unadjusted analysis were included in the multivariable analysis (log binomial regression) and adjusted PRs with 95% CIs were calculated.

## Results

**Social and Behavioural factors:**
- The mean age was 35 years (range:18-75) and 56% female.

- One fourth of HHC were living in slums and were using some form of tobacco (predominantly smokeless).

- Nearly one fifth of households had income less than 100 USD per month and were currently using alcohol.

- 47% had BMI $\geq$23kg/m^{2}.

- 12% percent had at least one TB symptom; 13 (2%) had bacteriologically confirmed PTB.

**Prevalence of Diabetes and Prediabetes:**
- 239 (37%) of 652 HHC had diabetes or prediabetes; 64 (10%) had diabetes and 175 (27%) had prediabetes.

- Of 64 HHC with diabetes, 40 (64%) were newly diagnosed by HbA1c screening. The majority (75%) of both known (17 of 24, 71%) and newly diagnosed (31 of 40, 78%) diabetes had poor glycemic control.(**Figure 1**).

- The mean$\pm$SD HbA1c among HHC with diabetes and prediabetes were 8.3%$\pm$2.0 and 6.0%$\pm$0.2, respectively. The distribution of HbA1c among HHC in **Figure 2.**

**Factors associated with diabetes:**
- HHC >= 35 years, those with BMI $\geq$25kg/m^{2}, having co-existing chronic diseases, those who smoked tobacco, and who lived in Tamil Nadu had significantly higher prevalence of diabetes (**Table 1**).

- In adjusted multivariable analysis, age >= 35 years, BMI $\geq$25kg/m^{2}, presence of chronic disease, and tobacco smoking remained significant for diabetes.

- We did not find any significant association/clustering of diabetes (PR 1.4; 95% CI 0.8 – 2.5) or prediabetes (PR 1.1; 95% CI 0.6 – 2.0) in our households.

**Association of diabetes and prediabetes with LTBI:**
- Overall, 78% of HHC had LTBI by either TST or QGIT (58% positive by TST, 61% by QGIT and 37% by both).

- We did not find any association between LTBI and diabetes or prediabetes among HHC. This remained consistent whether we defined the presence of LTBI by TST alone, QGIT alone or with both TST and QGIT combined.

**Table 1: Factors associated with diabetes among adult household contacts (HHC) of adult pulmonary TB patients in Chennai and Pune (recruited in CTRIUMPH study), India, 2014-2017**

| Variable | PR (95% CI) | Adjusted PR (95% CI) |
|---|---|---|
| **Sociodemographic characteristics** | | |
| **Age** | | |
| 18-34 | Ref | Ref |
| 35-44 | 7.5 (2.9 – 19.7) | 4.7 (1.8 – 12.2) |
| 45-54 | 11.6 (4.5 – 30) | 8.4 (3.2 – 22.1) |
| 55 and above | 16.6 (6.7 – 43) | 10.3(3.7 - 28.4) |
| **Gender** | | |
| Male | Ref | |
| Female | 0.9 (0.6 – 1.4) | |
| **Education** | | |
| Illiterate | Ref | |
| Primary (0-5 years) | 1.2 (0.6 – 2.5) | 1.3 (0.7 – 2.7) |
| High school (6-10 years) | 0.9 (0.5 – 1.7) | 1.4 (0.7 – 2.7) |
| 10+2, College and above | 0.4 (0.2 – 0.9) | 1.0 (0.4 – 2.4) |
| **Total Household income** | | |
| 1500 – 7499 | Ref | |
| 7500 - 11999 | 0.9 (0.5 – 1.8) | |
| 12000 – 17499 | 0.9 (0.4 – 1.8) | |
| 17500 and above | 1.2 (0.6 – 2.3) | |
| **Residence** | | |
| Rural | 0.8 (0.5 – 1.4) | 0.9 (0.6 – 1.6) |
| Slum | 0.4 (0.2 – 0.9) | 0.6 (0.2 – 1.1) |
| Urban | Ref | |
| **Relationship to Index case** | | |
| First degree relative | 1.0 (0.6 – 1.6) | |
| Others | Ref | |
| **Site** | | |
| Chennai | 1.8 (1.1 – 3.1) | 1.4 (0.7 – 2.6) |
| Pune | Ref | |
| **Tobacco Use** | | |
| Both Smoke+ smokeless | - | - |
| Smoke tobacco only | 2.4 (1.3 – 4.5) | 2.3 (1.2 – 4.5) |
| Smokeless tobacco only | 0.8 (0.4 – 1.6) | 0.6 (0.3 – 1.2) |
| No tobacco use | Ref | |
| **Alcohol use** | | |
| Risky drinking / Hazardous | 0.6 (0.3 – 1.5) | |
| Alcohol abuse / Harmful | 1.2 (0.5 – 3.1) | |
| Alcohol dependent | 1.8 (0.5 – 6.5) | |
| Never or Past user | Ref | |
| **Clinical Characteristics** | | |
| **Index DM status** | | |
| Prediabetes | 1.1 (0.6 – 2.1) | |
| Diabetes | 1.4 (0.8 – 2.5) | |
| Normoglycemia | Ref | |
| **Body Mass Index(kg/m^{2}))** | | |
| Under nutrition(< 18.5) | 0.5 (0.1 – 1.7) | 0.5 (0.2 – 1.8) |
| Normal (18.5 – 22.9) | Ref | |
| Overweight (23-24.99) | 1.6 (0.7 – 3.7) | 1.4 (0.7 – 3.0) |
| Obesity (≥25) | 2.8 (1.5 – 5.1) | 2.1 (1.2 – 3.6) |
| **Chronic Disease** | | |
| Chronic Disease | 3.4 (2.3 – 6.0) | 1.7 (1.0 – 3.0) |
| No chronic disease | Ref | |
| **HIV** | | |
| Positive | - | |
| Negative | Ref | |
| **Latent TB Infection** | | |
| Positive | 0.8 (0.5 – 1.4) | |
| Negative | Ref | |
| **TB symptoms** | | |
| Symptoms | 0.9 (0.4 – 1.9) | |
| No symptoms | Ref | |
| **TB disease** | | |
| Yes | 0.8 (0.1 – 5.2) | |
| No | Ref | |
| **Diabetes of Index TB patient** | | |
| Prediabetes | 1.1 (0.6 – 2.0) | |
| Diabetes | 1.4 (0.8 – 2.5) | |
| Normoglycemia | Ref | |

CTRIUMPH=Cohort for TB Research with Indo-US Medical partnership; TB=Tuberculosis; DM=Diabetes Mellitus; HIV=Human Immunodeficiency Virus; HbA1c=Glycosylated Haemoglobin; Pre-DM=Prediabetes; INR=Indian National Rupees; TST=Tuberculin Skin test; QGIT= QuantiFERON®-TB Gold in Tube test; PR=Prevalence Ratio; CI=Confidence Intervals; Ref=Reference category; kg=Kilograms; m=meters
BMI classification according to the Indian Consensus Group (for Asian Indians residing in India)[2]: Under nutrition(< 18.5), Normal (18.5 – 22.9), Overweight (23-24.99), Obesity (≥25)

**Figure 1. Prevalence of diabetes and prediabetes among adult household contacts (HHC) of pulmonary TB patients in Chennai and Pune (recruited in CTRIUMPH study), India, 2014-2017**



CTRIUMPH=Cohort for TB Research with Indo-US Medical Partnership; TB=Tuberculosis; DM=Diabetes Mellitus; HbA1c=Glycosylated Haemoglobin; HHC=Household contacts; Poor glycemic control = HbA1c > 7.0%; Known DM = Previously diagnosed self-reported diabetes mellitus
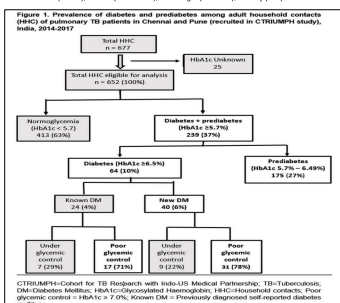
**Figure 2. Distribution of HbA1c% among adult household contacts (HHC) of pulmonary TB patients in Chennai and Pune (recruited in CTRIUMPH study), India, 2014-2017**



**Legend:** A total of 417 (64%) HHC had HbA1c less than 5.7%, 178 (27%) had HbA1c between 5.7% and 6.4% meeting screening criteria for prediabetes, and 57 (9%) had A1c 6.5% or higher.

## Conclusion

- Our study, is among the first to assess the prevalence of diabetes and prediabetes among HHC of TB patients using systematic HbA1c screening in a high TB and diabetes burden setting.

- Nearly four in ten HHC had diabetes or prediabetes. Most individuals were unaware of their diabetes and prediabetes diagnosis.

- Furthermore, among both known and newly detected diabetes, 75% had poor glycemic control (HbA1c $\geq$ 7% ).

- Finding nearly 40% of adult HHC with diabetes or prediabetes was higher than expected, compared to what was observed in the general adult population of India and in many high-income settings.

- HbA1c $\geq$ 7% is associated with a 2-3 fold higher risk of developing TB and is also associated with increased risk of diabetes-related micro and macro-vascular complications.

- Finding such high rates of diabetes and prediabetes among HHC recently exposed to TB patients in a high TB burden setting is alarming, and likely represents a critical missed opportunity for both TB prevention and early detection of diabetes.

- Further studies are needed to determine if identifying and targeting preventive therapy for this high risk group of contacts will be of particular benefit.

**Limitations:**
- Diabetes diagnoses by HbA1c generally requires a second test to confirm the presence or absence of diabetes. Therefore we may have misclassified a few persons with diabetes and prediabetes relying on a single HbA1c result.

- We missed enrolling about 20% of the eligible HHC for various reasons and we are not able to assess if these HHC were or were not similar to those enrolled.

## Recommendations

- Nearly four in ten HHC of TB patients had diabetes or prediabetes and ~80% had LTBI.

- Given the potential for TB prevention and future diabetes prevention, routine diabetes screening may be of great benefit to adult HHC.

- Targeted preventive therapy for HHC with diabetes and prediabetes, should be considered.

## Acknowledgements