

Association between Diabetes Mellitus and Tuberculosis as a Global Issue

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Abstract:- Diabetes mellitus and tuberculosis are chronic diseases and their association is existing for thousands of years, although association is not causal, but precipitating to each other. As systemic reviews of many global databases suggest that diabetes mellitus increases the risk of tuberculosis three times & tuberculosis impairs the glucose tolerance levels (GTT), which in turn can lead to pre-diabetic stage & then diabetes mellitus. As per WHO report of 2014 there were 422 millions of diabetes mellitus cases in the world. It's likely to reach 624 millions by 2040. There are 14.6 millions of tuberculosis cases & around 1.6 millions tuberculosis patients die each yr. Global databases suggests that there are 15% diabetics are associated with tuberculosis & 80-90% diabetic and tuberculosis patients are found in developing countries due to poverty, malnutrition, poor health & sanitation, political instability & govt's lackadaisical attitude. present strategy for screening, diagnosis & management of TB and diabetes mellitus is not halting the progression of Tuberculosis & diabetes, so we have to devise new strategy based on research and latest technology to deal with combo challenges, we have to make it compulsory for bidirectional screening, proper diagnosis & treatment & complete follow up of all the cases.

I. INTRODUCTION

Tuberculosis & diabetes mellitus are chronic diseases challenging the human beings survival from pre-neolithic era to Modern human beings, earliest evidence of tuberculosis have been found in mummy of 30yrs old woman in 5803 BC in Italy & another evidence of pthisis (TB) found in 4803 BC in Egypt & in 1552 BC Egyptian physician HESY-RA described hyperglycemia, another Indian physicians named CHARAK & SASRUTA described the comorbidity features of diabetes mellitus & tuberculosis as madhumeha and pthisis as; meganicola. (44)

First documented study describing association between diabetes mellitus and tuberculosis patients was done in neolithic era in 11th century by Arabian physician and philosopher named AVICENNA (24). As per WHO report of 2014 there are 422 millions of diabetes mellitus cases all over the world, & globally prevalence of diabetes mellitus cases have doubled from 1980- to 2014 from 108 millions with prevalence rate 4.7% to 422 millions with prevalence rate 8.4% respectively. It is

expected that with prevalence rate of 8.4% it will reach to 640 millions by 2040AD.

In 2016 there were 14.6 millions tuberculosis patients, out of which 1.6 millions died in a yr (4).

A cohort study in taiwanese have 123546 participants with five year follow up period, suggest that poor glycemic control have doubled the rate of development tuberculosis (14) another case control study done in Salvador, bawi, Brazil between 2008 to 2010 which recruited 323 new cases of tuberculosis have positive bacilloscopy test & similar number as control group with negative bacilloscopy test, OR-odds -Ratio found it is - 2.37 95% CI (1.04-5.42) as per global databases 15% of diabetic are associated with tuberculosis. Till date WHO have highlighted the impending doom of diabetes mellitus and tuberculosis as emerging challenge to Modern world. so WHO have cautioned the developing & high risk countries to adopt good clinical practices for cure & management of tuberculosis & diabetes mellitus. In spite of latest technology and new medicines, both tuberculosis & diabetes mellitus are spreading at alarming rate for which we need a comprehensive result oriented strategy to control menace of tuberculosis & diabetes mellitus.

II. METHOD

pubmed & Google scholar databases were thoroughly searched using topics as diabetes mellitus & tuberculosis association, incidence, prevalence rate, their manifestations mortality & morbidity rate, treatment outcomes are traced on excell worksheet.

III. RESULT

we have observed from the global databases studies that 15 percentage of diabetics are associated with tuberculosis although there is no evidence of any causal relationship. So there should be bidirectional screening of diabetes mellitus & tuberculosis.

Diabetes mellitus--epidemiological aspects --hesy-ra Egyptian physician was The first in 1552 B.C to mention the hyperglycemia, what we name now a days as Diabetes mellitus, in 1500 B.C Indian physicians named CHARAK & SUSRUTA described The mysterious emaciating disease as Madhumeha

(23) in which urine of patient usually attracted ant's, then afterwards patients were diagnosed by taste of their urine, but time being there was no exact scientific & evidence based therapy, finally in 1922 in Canada at Toronto based general hospital insulin extract was given by parenteral route & results were remarkable, in 1955 first generation oral antidiabetic drug's were introduced.

As per W.H.O report of 2014 there were 422 million diabetics in the world & since then diabetes mellitus have increased exponentially as evident from 1980 report have 108 million diabetics at prevalence rate 4.7 percentage which have doubled in 2014 to 422 million at prevalence rate 8.5 percentage & 1.6 million diabetics have died in 2015 by diabetes mellitus and its complications (3).

Tuberculosis--epidemiological aspects--following is the estimated statistics report as per

- W.H.O survey of 2016yr
- Africa--417000
- America --17000
- Eastern Mediterranean--82000
- Europe--26000
- South east asia 652000
- Western Pacific--103000

Tuberculosis is chronic highly infectious disease since prehistoric era creating havoc & devastation, disability of human beings (27). In ancient Greece tuberculosis was called as phthisis & in ancient Rome named as tabes, Schache peth in ancient Hebrew, in 1700 A.D tuberculosis was called as White plague due to paleness of patients, in 1834 A.D Schonlein coined the term tuberculosis, in 1882 A.D Dr Robert Koch first discovered mycobacterium tubercule bacilli as the causative agent of tuberculosis in human beings, in modern era tuberculosis have variants like pulmonary TB, extrapulmonary TB, drug resistant like MDR, XDR tuberculosis etc. (29). 95% deaths due to Tuberculosis occurs in lower & middle income countries, out of which 65% deaths were in male adults. Global view of the seven countries account for 64% of total TB cases & India is frontrunner out of them followed by Indonesia, China, Pakistan, Philippines, Nigeria, Mozambique,

Now India have devised New strategy that is END-TB strategy goal 2025, for which India have to achieve target of 4-5% annual fall of Tuberculosis incidence rate, as presently India have 2% annual fall of Tuberculosis incidence rate.

Association of Tuberculosis & diabetes mellitus ---on The global level there were 10.6 million active TB patients in the 2016 & about one million have TB and diabetes mellitus as combined & 15% TB cases are confined to diabetes mellitus (2)

First work on association of diabetes mellitus and Tuberculosis was done by AVICENNA-a Persian philosopher & physician in 980 to 1052 A.D, diabetes mellitus increases the risk of Tuberculosis by three times (24).

IV. DISCUSSION

Diabetes mellitus a risk factor for Tuberculosis--patients with uncontrolled hyperglycemia are at risk of developing Tuberculosis three times as compared to general population. A cohort study in Barcelona from 2000 to 2013 with 5849 TB patients, out of which 349 (5.9%) have diabetes mellitus, over 14 yrs follow up period, diabetes mellitus prevalence rate was 4% to 7.3% with (Ci)- interval 95% however management of tuberculosis patients with diabetes mellitus was more complicated. (34).

Another cohort study using databases from United Kingdom clinical practice research datalink of 222731 patients with diabetes mellitus diagnosed over 1990 to 2013, control group have 1218616 subjects without Tuberculosis, over a period of 24 yrs it was observed that the Tuberculosis incidence rate was higher in diabetics as compared with control group 16.2% per lac in diabetics & 13.5% in control group.

A case control study conducted in Salvador, Bawia Brazil from 2000 to 2010 which recruited 323 new cases of tuberculosis with positive bacilloscopy test & similar number of control group with negative bacilloscopy, then (odds ratio) O.R- was observed as --2.37 C.I (confident interval) 95% --(1.04-5.42) which shows very significant association between Tuberculosis & diabetes mellitus (36).

Another longitudinal cohort study done in Chile from 1959 to 1982 prospectively with 10 yrs follow up period revealed Tuberculosis incidence 24% in IDDM (insulin dependent diabetes mellitus) & 4.8% in type 2 diabetes mellitus patients (9).

RADIOLOGICAL Presentation in pulmonary Koch's with diabetes mellitus--total 50 patients of pulmonary Tuberculosis who were on insulin or oral hypoglycemic drug's & have (FBS) fasting blood sugar More than 140mg on two or more occasions were included in this group

84% patients have lower lung Fields involvement while 16% have upper lobe involvement, 32% have bilateral involvement, 68% have unilateral involvement, 20% have cavitary Tuberculosis lung disease & 80% cavitary lung disease lesions were confined to lower lung Fields (17).

SPUTUM SMEAR conversion-- A retrospective descriptive study done in FIJI from 2010 to 2012 in which 577 Tuberculosis patients were recruited, out of which 567 (98%) have information regarding Tuberculosis, & 68 (12%) have diabetes mellitus also, sputum smear conversion rate after two

months of intensive phase treatment was non significant & equivalent to Tuberculosis patients with or without diabetes mellitus 78%Versus80% $p=0.66$, although diabetes mellitus is common in Tuberculosis patients but conversion rate was non significant (18).

Another retrospective cohort study done in Tamil Nadu district hospital Tiruchirapalli from November 2015 to March 2016 in which 1131 Tuberculosis patients treatment cards were selected, out of which 14% (163/1131) were documented as Tuberculosis plus diabetes mellitus patients & out of 114 diabetes mellitus plus Tuberculosis sputum positive patients, 107 (94%) had smear conversion at the end 2nd month of intensive phase & three patients have smear conversion at the end of extended intensive phase treatment (39).

Pharmacological drug interactions in Co - management of Diabetes mellitus & Tuberculosis---patients diabetes mellitus & Tuberculosis should be managed by insulins, sulfonylureas, thiazolidinediones -pioglitazones, rosiglitazones, incretins agonists (45) (GLP-1) glucagon like peptide receptor agonists such as exenatide -liraglutides, DPP-4 inhibitors such as sitagliptin, saxagliptin, alogliptin, & vildagliptin have interactions with rifampicins & isoniazid (40).

As rifampicin is a hepatic enzyme inducer, so it lowers the plasma level of sulfonylureas, biguanides & thiazolidinediones leading to hyperglycemia in diabetes mellitus patients, where as isoniazid inhibits metabolism of sulfonylureas leading to the uncontrollable hypoglycemia (42).

V. CONCLUSION

As per data for diabetes mellitus & Tuberculosis studies on Google & pubmed scholar, it's suggested that both diabetes mellitus & Tuberculosis are precipitating to each other, although there's no evidence of any causal relationship, but 15% of diabetics are associated with tuberculosis. so tackling this double challenge there should be a bidirectional screening of diabetes mellitus & Tuberculosis, special focus should be on management strategy, nutritional support and intersectoral coordination, govt's sincerity etc. there are still many unanswered questions like 1) why there is increase in incidence of Tuberculosis in diabetes mellitus & vice versa in developing world, (2) what are the exact causes of treatment failure, relapse of cases in both Tuberculosis & diabetes mellitus patients etc.

REFERENCES

- [1]. RNTC programe--india-- National strategic plan for Tuberculosis eradication 2017-2025
- [2]. Zheng chunlan, Minhui-Hu, Gad Feng--Diabetes mellitus & pulmonary Tuberculosis global overview, special focus on high TB-diabetes burden, Pub.online jan13-2017.
- [3]. Fatima-mukhtar, Butt-A Zahid--Cohort profile --diabetes mellitus-tuberculosis, BMJ-open(02 December 2016,6(12)e012970) Doi:-10.1136/bmj open 201601290.
- [4]. world health organization- global report on diabetes mellitus 2016,. (<http://www.who.int>)
- [5]. world health organization underscores action needed against Tuberculosis & diabetes: world diabetes foundation summit in Bali, 28 October 2015, www.worlddiabetesfoundation.org
- [6]. world health organization:-stresses urgent need for research and development for drug resistant to alongside newly prioritized antibiotic resistant pathogens, 27 February 2017.
- [7]. Kotterath-Manoj, Rajni vovila, A chuthan.v et Al. --prevalence of diabetes mellitus in Tuberculosis patients a hospital based study, Doi:- http://dx.doi.org/10.18203/2320-6012_ijrms--2015 international journal of research in medical sciences.
- [8]. Dobler Claudia Carolin, Ronald Jeffery flack, Marks Guybouryer-- Risk of Tuberculosis among people with Diabetes mellitus:- Australian Nationwide cohort study, <http://dx.doi.org/10.1136/bmj open--2011000666>.
- [9]. Suwanpi molkal-Gompol, Grinsdale Jennifer A, et al, association between diabetes mellitus and Tuberculosis in USA born & foreign -born population in San Francisco, published on 05 December 2014, doi 10.1371/journal.pone.0114442, Pmcid:pmc4257695, pmid 25478954.
- [10]. Holt I.G Richard, Clive's cockery, Allan- Fuyubjerg, Barr J Goldsten --Text book of Diabetes mellitus 4th edition.
- [11]. Tuberculosis & cultural competency notes from the field issue family affair # 11 June 2010, New Jersey Medical school global Tuberculosis institute, 225 women street, New Jersey 07101-1709 973972 3210.
- [12]. Adela Gabriella Firanesc, Adine popa, Maria-Magdalena Sandu, Diana Cristina, Maria Motu, et al - The global prevalence & incidence of diabetes mellitus & pulmonary Tuberculosis <http://rjdnm.org/index.php/RJDNMD/article/view/87> issue vol 23, no 3 (2016).
- [13]. Autoren, Xiang-han, Qiuzhen Wang Yang- Wang, Jina Lai et al. The impact of Diabetes mellitus on Tuberculosis treatment outcomes: evidence based on a cumulative meta analysis-- Zeitschrift international journal of Diabetes mellitus in developing countries AUSGABE 4/2016.
- [14]. Pin- Hu, Lee Han-Fu#1, Ting chunlai#2, Chang chuan-chun#3, Hsien-ho-lia--Glycemic control & rise of Tuberculosis- a cohort study.
- [15]. Enrico Giardi, Monica Sam Schepisi, Delia-Golett, Matthew-Dates, - - Global Dynamics of diabetes mellitus & Tuberculosis, The impact of migration & policy implications.
- [16]. W.H.O--Global report 2016 on diabetes mellitus--ISBN--9789241565257 N.C.Mclassification Wk 810.

- [17]. Anand-K- Patel, Kiran. C .Rami,Feroz-D-Ghanchi -- Radiological presentation of patients of pulmonary Tuberculosis with Diabetes mellitus.
- [18]. Prasad-P,Gounder-S,Vanel-K --Sputum smear conversion & treatment outcomes for Tuberculosis patients with & without diabetes mellitus in Fiji.
- [19]. Harris-A.D , Kumar-A.M.V , Kapoor-A,-- diabetes mellitus & Tuberculosis programmatic management issue, international journal of Tuberculosis & lung diseases 2015 Aug. 19(8) 8795886 doi 10.5588/IJTD 15.0069,. PMCId,pmc 4497633,. Pmid 26162352.
- [20]. Chen-Yuan-Chiang, jen- Jyr-Lee, Shun- Tian chien, Donald- Enarson,--Glycemic control and RADIOLOGICAL manifestations Tuberculosis in diabetes mellitus patients.
- [21]. Susan Martin perera, Gleide Santos-de, Aranuj(--)mauriliz Lima barreto, Rev Sande,. -publication 2016,58;82, published online 2016nov 24,. Doi 20.1590/51518-8787, PMCId-pmc 0152-831-pmid28099656.
- [22]. Kelly Dooley md PhD, John hopkin University school of medicine--centre for AIDS research, John hopkin University drug-drug interactions in Tuberculosis & diabetes-11may 2016 in HIV and Tuberculosis patients.
- [23]. Mark stellner, Danieta Steinberg, Christian.J Hartman, Taijana Pabst,Lidija konta,Hans Peter hartung, bernard.c Kiessier,--isonizid induced polyneuropathy in Tuberculosis patients. 2015 August,5(8)000326published online 2015may 26,doi10/002/brb,3.326,. Pmcid--pmc4559012-pmid26355945.
- [24]. Richard-I G.holt, Wiley blokewell, Clives-cockram,Allan-Flybjerg,Barry-j Goldstein,.History of Diabetes mellitus ISBN-978-405/9181 --2010.
- [25]. Huang Kuo-li, Hsueh Wang,Yichun lai, Shi Chilan chang--The impact of glycemic status & Radiological manifestations of pulmonary Tuberculosis in diabetes mellitus patients.
- [26]. Liu-Q. Li-w, Xue-M, Chen-Y, Du-x, Wang-C, Han-L, Tang Y, Feng Y, Taoc,etAl--Diabetes mellitus & Risk of multidrug resistant Tuberculosis:- A meta analysis. Doi:10.1038/5 41598--017-1213-5, published online 24/04/2017.
- [27]. W.H.O-department of communication Geneva--global Tuberculosis report 2017.
- [28]. C.D.C-information USA-Govt. Center for disease control and prevention, December 12-2016, updated march16-2018.
- [29]. www.w.h.o.int., Tuberculosis 16 Feb 2018.
- [30]. BLanca-i-Restrado, U.T health Houston school of public health at Brownsville,80 Fact Brown,Texas 78520, published in 2016 December.
- [31]. <https://en.wikipedia.org>,Avicena Wikipedia.
- [32]. Magna manjareeka, subrata Kumari polo, sangamitra pati ,--journal of clinical &diagnostic research:- Prevalence of Diabetes mellitus in newly diagnosed pulmonary Tuberculosis in tribal odisha, published online 2016 October, doi-10.7860/jcDR/2016/20999.8704 PMCId-pmc 5121697, pmid27891359.
- [33]. Travis-B Nielsen,Paul pants palangkoor, Jun yan, Brian-M - Luna ,Kev Dekitani, Kevin Bruhn, Brandan Tana, Justin Junas Robert-A Bononio, Ann Maril Schmidt, Terenle-M- Dohertye,lin- Lin ,et al. - Diabetes mellitus exacerbates infection via hyperinflammation by signalling there on TLR4 & REGE.
- [34]. Moreno Martinez-A ,Casals-M, Orcan -A --factors associated with Diabetes mellitus among adults with tuberculosis in a large European City-2000 to 2013 , international journal of Tuberculosis & lung diseases, 2015; 1911507-1512, doi:10.5588 , ijtld 15.01102(pubmed).
- [35]. Louise pealing,Kevin wing,Mathur Rohini, David A.J Moore,. --BMC medical2015,13:135 doi 10.1186/s12/6-015 2331.9 Pmcid; PMC 4470065 , pmid;26048371, Faculty of infectious & tropical diseases, London school of hygiene & tropical medicine.
- [36]. Cheng-chen, limei Zhu , Dhandan- yang, yan shao, Sona hon Ghuan ,Gyolici Wlei-lu, --Risk factor's association with tuberculosis--a case control study in a Chinese population.
- [37]. Denise-Martinez Dleguera,Rafael laniado laborin. -- Glycemic control & rate of sputum conversion in diabetics patients with Tuberculosis, Received December 2015, published feb 2016
- [38]. Velayutham-banurekha, Bhatnagar Tarun, Swaminathan savitri, Natrajan Dinesh Kumar,Bupasthi Kangu Samy --tuberculosis control programme in Urban setting, south India, Indian journal of community medicine,official publication of Indian association of preventive & social medicine,--Sputum conversion & treatment success amongst Tuberculosis patients with Diabetes mellitus treatment outcomes under TCP .
- [39]. Anc Lelia Riza, Fiona Pearson, Cesar Ugarte-giza, Bacti Alisjahbana, Steven Vande- Vijver, Nicolaem panduru, Philip-c-hill ,Rovina qussami, David Moore,Rob Aornoutse et al--clinical management of concurant diabetes mellitus & Tuberculosis & the implications for patients service, published in the lancet diabetes mellitus endocrinology 12 September 2014, doi10.1016/52213-8587(14)70110.
- [40]. Rovina Ruslima, Honnoke-M.J Nijland, I. Gusti-N adhiarta, Shri H.K.S kariadi, Bacti Alisjahbana, Roble Arnaustse, Reinor Van crenel --pharmacokinetics of antitubercular drugs in pulmonary Tuberculosis patients with type - 2 diabetes mellitus.

- [41]. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3598170/>, Ak niazi 2012-december20th., Kalra Sanjay.--Diabetes mellitus & Tuberculosis review of the- role of optimal Glycemic control--published online 2012 December 20th., Doi-co 1186/2251--6581-11--88 ,pmc-id--pmc3598170--pmid23497638.
- [42]. :Requene Mendez,. Davis G,. Andrey. A,. javel-o, Lopez Romerosl, Ward SA, MooreDA --pharmacokinetics of rifampicin in Peruvian Tuberculosis patients with or without comorbid diabetes mellitus or HIV Doi 10.1120/AAC.66059--11,--2012.
- [43]. Cristine Morazzon, Massimo Depaschale --published 30th June 2016 Doi 104081,.20165782.
- [44]. Richard I.G Holt, Clive-S cockram , Allan-Flyvbjerga, Barry J. Goldstein.-- textbook ofDiabetes mellitus.