**CORRELATION BETWEEN CARDIOVASCULAR DISEASE AND PULMONARY FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A LITERATURE REVIEW**

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**ABSTRACT**

The prevalence of diabetes in India has been steadily increase over the past few decades, making it a major public health concern. American Thoracic Society European Respiratory Society (ATS/ERS guidelines) demonstrates that the lungs should also be considered as a primary target organ for diabetic complications along with other micro- and macrovascular complications. There was a significant decrease in FVC, FEV1, and PEFR, and a dominant restrictive pattern of pulmonary dysfunction was observed in type 2 diabetes mellitus. Multiple studies have shown a high prevalence of cardiovascular complications at the initial diagnosis of type 2 diabetes.

This study addresses the existing gap in literature by investigating the correlation between cardiovascular disease and pulmonary function in patients with type 2 diabetes. The study aims to contribute to the understanding of the interplay between these conditions, provide insights into their coexistence and potential implications for patient’s management and ultimately improve the overall care and outcome of individuals with type 2 diabetes.

Our study involved a search that encompassed 40 articles, followed by meticulous screening to select 18 articles meeting our predefined inclusion and exclusion criteria. These chosen articles formed the basis of our comprehensive literature review.

Our review did not identify any studies that have investigated the correlation between risks of cardiovascular disease and pulmonary function in individuals with type 2 diabetes mellitus.

**INTRODUCTION**

The prevalence of diabetes in India has been steadily increase over the past few decades, making it a major public health concern(Pradeep R, 2021). Diabetes is a chronic metabolic disorder characterized by elevated blood sugar levels and can lead to serious complications if not managed properly (Mittal S et. Al, 2023, Clive R Hamlin, 1975).

Type 2 diabetes is the most common form of diabetes in India, accounting for over 90% of all cases, it is primarily a lifestyle-related disease, where the body becomes resistant to insulin the hormone that regulates blood sugar or doesn’t produce enough insulin to maintain normal blood sugar levels. Risk factors for type 2 diabetes in India include obesity, sedentary lifestyle, unhealthy diets, family history, and ethnicity (Pradeep R, 2021, Fogarty et al, 2007)

The escalating global burden of diabetes necessitates further research into its impact on pulmonary functions. The lungs substantial blood supply, comprising about ten percent of the body's circulatory system, makes them susceptible to the effects of chronic hyperglycemia on-enzymatic glycosylation of proteins like collagen and elastin due to high blood sugar levels thickens the basement membrane and causes microangiopathy. Given diabetes' known detrimental effects on microvasculature, it is highly plausible that pulmonary functions may be compromised in individuals with diabetes mellitus. Therefore, comprehensive studies are crucial to understand and address the potential consequences of this multi-systemic disease on respiratory health (Nabel EG, 2003)

American Thoracic Society European Respiratory Society (ATS/ERS guidelines) demonstrates that the lungs should also be considered as a primary target organ for diabetic complications along with other micro- and macrovascular complications. There was a significant decrease in FVC, FEV1, and PEFR, and a dominant restrictive pattern of pulmonary dysfunction was observed in type 2 diabetes mellitus The exact pathophysiology for reduced pulmonary functions in diabetes mellitus is still an interesting area of research and more prospective studies in larger populations should be performed using advanced techniques to include this as a long-term complication of diabetes mellitus (ATS/ERS 2022).

Multiple studies have shown a high prevalence of cardiovascular complications at the initial diagnosis of type 2 diabetes (ATS/ERS 2022). These complications, such as hypertension, altherosclerosis and heart disease, can occur even before the formal diagnosis, highlighting the importance of early detection and comprehensive management strategies to minimize cardiovascular risks in diabetic patient (Stratton et al. 2000).

Cardiovascular disease is the leading cause of illness and death worldwide, imposing substantial healthcare cost (Ghosal S et al 2020). It prevalence places a heavy burden on healthcare systems, requiring significant resources for prevention, diagnosis and treatment. Addressing this major health challenge is crucial to reduce mortality rates ans alleviate the economic strain on healthcare infrastructure (Rawshani A et al, 2017).

Cardiovascular disease (CVD) is mainly influenced by controllable risk factors like high cholesterol, hypertension, obesity, smoking, inactivity and diabetes. Implementing lifestyle changes, managing these factors through treatment and adopting healthier habits can significantly reduce the risk of CVD and improve overall heart health (Cosentino F et al, 2020) Pulmonary function tests (PFTS) are an important tool in the investigation and monitoring of patients with respiratory pathology. They provide important information relating to the large and small airways, the pulmonary parenchyma and the size and integrity of the pulmonary capillary bed. Parameters assessed were – Force vital capacity (FVC) in litres, Force expiratory volume in 1 second (FEV1), FEV1/FVC and Peak expiratory flow rate (PEFR) (Davis et al, 2004). The QRISK3 score served as the principal metric for evaluation in the study. Utilizing a sophisticated statistical model, the researchers calculated the QRISK3 score to assess the participants overall risk of developing a particular health condition. This score provides information on CVD absolute and relative risks over a 10-years period (Hippisley Cox et al, 2017).

**METHODOLOGY-**

**Search Strategy:**

A comprehensive search of relevant literature was conducted using electronic databases such as PubMed, MEDLINE, Scopus, and Web of Science. Keywords and phrases were included "Type 2 Diabetes Mellitus," "cardiovascular disease," "Pulmonary Function," "Correlation," "Mechanisms," and related terms. Boolean operators (AND, OR) were used to combine keywords appropriately.

**Inclusion and Exclusion Criteria:**

Inclusion criteria:

* Research articles published in peer-reviewed journals.
* Studies focusing on the correlation between cardiovascular disease and pulmonary function in patients with Type 2 Diabetes Mellitus.
* Studies published in English.
* Studies conducted on human subjects.

Exclusion criteria:

* Opinion, and conference abstracts.
* Studies that do not directly address the correlation between cardiovascular disease and pulmonary function.
* Studies conducted on animal models or non-human subjects.
* Non-English studies.

The identified articles were undergo a two-stage selection process. In the first stage, titles and abstracts were screened to determine their relevance to the research question. In the second stage, full-text articles were assessed against the inclusion and exclusion criteria.

Relevant data from the selected articles will be extracted using a standardized data extraction form. Information to be extracted includes study design, sample size, participant characteristics, methodologies used to assess cardiovascular disease and pulmonary function, key findings related to the correlation, and potential mechanisms explored.

**PREVALENCE OF DIABETES MELLITUS IN INDIA**

Diabetes has emerged as a significant global health crisis in the current century, securing a place among the top 10 primary contributors to mortality alongside cardiovascular disease (CVD), respiratory disorders, and cancer. Over the observed period from 2009 to 2019, the prevalence of diabetes in India has undergone an escalation from 7.1% to 8.9%. At present, the estimated number of adults affected by impaired glucose tolerance (IGT) stands at 25.2 million, a figure projected to elevate to 35.7 million by the year 2045. In the worldwide landscape of diabetes incidence, India holds the second position, trailing only China, with a significant diabetic population of 77 million individuals.

**PULMONARY FUNCTION VARIATIONS IN TYPE 2 DIABETES MELLITUS VS. NON-DIABETIC INDIVIDUALS**

The ratio of Forced Expiratory Volume in one second to Forced Vital Capacity (FEV1/FVC %) exhibited a notable increase among individuals diagnosed with type 2 diabetes in comparison to the control group. This observed rise was established to possess statistical significance. The elevated FEV1/FVC % values pointedly indicated that the compromised pulmonary functions among type 2 diabetics predominantly exhibited a character of restriction. This pattern aligns with findings from a separate study, wherein the ratio was identified to experience a statistically significant increment of 1.5% in diabetic subjects.

**PULMONARY FUNCTION IN TYPE 1 AND TYPE 2 DIABETES MELLITUS: INSIGHTS FROM CLINICAL STUDIES**

In their research titled "Associations of Measures of Lung Function with Insulin Resistance and Type 2 Diabetes," D. A. Lawlor, S. Ebrahim, and G. Davey Smith explored the relationship between lung function measures and insulin resistance. The British Women's Heart and Health Study findings revealed an intriguing inverse association between lung volume-related measures of lung function and insulin resistance, as well as Type 2 diabetes. This correlation could potentially be attributed to childhood exposures impacting lung growth and influencing the programming of insulin resistance.

Similarly, in the study "Pulmonary Function in Patients with Diabetes Mellitus" conducted by CARLOS A. BENBASSAT, MD; ERVIN STERN, MD; MORDECHAI KRAMER, MD; JOSEPH LEBZELTER, PHD; ILANA BLUM, MD; and GERSHON FINK, MD, spirometric values were scrutinized in diabetes mellitus patients. Their findings indicated that spirometric values remained relatively unaffected in these patients, with no discernible deficits in diffusing capacity. However, they suggested that impaired physical performance might be attributed to cardiovascular factors. Consequently, this research concluded that routine pulmonary function screening among diabetic patients might not be necessary.

Furthermore, the study "Effect of Glycemic Status on Lung Function Tests in Type 2 Diabetes Mellitus" by S N Naithok Jamatia, Kanan Wangkheimayum, W Asoka Singh, and Govindaraj Yumnam delved into the impact of glycemic status on lung function tests in type 2 diabetes mellitus patients. The study demonstrated a statistically significant correlation between glycemic status and impaired lung function, particularly in the form of a restrictive pattern. Notably, the correlations between postprandial blood sugar levels and forced vital capacity (FVC) were particularly pronounced. Moreover, the study identified a significant negative correlation between hemoglobin A1c (HbA1c) levels and both FVC and forced expiratory volume in one second (FEV1). These findings suggest a definitive association between glycemic status and diminished lung function, prompting the need for further research to elucidate the underlying pathophysiological mechanisms.

**CARDIOVASCULAR RISK IN TYPE 2 DIABETES MELLITUS**

The relationship between type 2 diabetes and cardiovascular disease (CVD) risk is well-established, with diabetes serving as a significant risk factor for the development of CVD. This risk is attributed to various factors, including insulin resistance, chronic hyperglycaemia, dyslipidaemia, systemic inflammation, and endothelial dysfunction. These mechanisms collectively contribute to the progression of atherosclerosis, thereby increasing the likelihood of coronary artery disease, myocardial infarction, and stroke. Understanding these complex connections is essential for designing targeted interventions to mitigate CVD risk in individuals with type 2 diabetes.

**RESULTS**

The outcomes of this comprehensive review underscore several significant trends in the context of pulmonary function among individuals with type 2 diabetes. Remarkably, various measurements within the spectrum of pulmonary function tests exhibited noticeable declines in this cohort, with the exception of the FEV1/FVC ratio. Particularly noteworthy were the substantial decreases observed in parameters such as forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and maximal voluntary ventilation (MVV). These findings illuminate the potential impairment in lung capacity and respiratory efficiency associated with type 2 diabetes.

It is crucial to emphasize that individuals recently diagnosed with type 2 diabetes face heightened susceptibility to cardiovascular complications and elevated mortality rates when compared to those without diabetes. However, it's noteworthy that, to date, no scientific investigation has specifically elucidated the correlation between cardiovascular disease risk and pulmonary function in the context of type 2 diabetes mellitus patients. The scarcity of such studies underscores the need for further research to bridge this critical knowledge gap and provide a comprehensive understanding of the intricate interplay between pulmonary function and cardiovascular risk within this patient population.

**DISCUSSION**

The findings from this study provide valuable insights into the relationship between pulmonary function and type 2 diabetes mellitus (T2DM). A notable decline in the majority of parameters within pulmonary function tests was observed among subjects with T2DM, with the exception of the FEV1/FVC ratio, which exhibited a significant increase. Particularly substantial reductions were evident in the values of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and maximal voluntary ventilation (MVV). Furthermore, it is worth noting that although slow vital capacity (SVC) displayed a decline in diabetic subjects, this decline did not reach statistical significance.

The current study's findings align with earlier research that also reported diminished vital capacity and a restrictive pattern among individuals with T2DM. Notably, recent investigations by Swati Mittal et al concluded similar outcomes, demonstrating significantly lower values of FVC, FEV1, and FEF25-75%. Additionally, the work by Irene M. Stratton et al highlighted an increased incidence rate for microvascular endpoints associated with rising glycaemia, surpassing the rate of increase in myocardial infarction incidence.

These observations are consistent with Samit Ghosal et al's study, revealing a pronounced 10-year cardiovascular disease (CVD) risk among T2DM patients. Similarly, Wendy A. Davis et al's Fremantle Diabetes Study underscored a decline in FVC, FEV1, vital capacity (VC), and peak expiratory flow (PEF) in patients with T2DM.

The congruence between the findings of this study and the aforementioned research underscores the consistent association between T2DM and compromised pulmonary function, particularly in measures of lung volume. The increased FEV1/FVC ratio in T2DM subjects warrants further investigation, potentially indicating an adaptive response or underlying pathophysiological mechanisms. These findings collectively emphasize the importance of closely monitoring pulmonary function in individuals with T2DM, as it may offer insights into their overall health status and susceptibility to cardiovascular complications.

**CONCLUSION**

The study's findings reveal that the lungs should be considered as a key target for complications in diabetes, just like other small and large blood vessel issues. People with type 2 diabetes experienced notable decreases in lung measures like FVC, FEV1, FEF 25-75%, and MVV. They showed a specific pattern of lung trouble called "restrictive," where their lungs didn't work as well as in healthy individuals. The exact reasons behind these lung issues in diabetes are still being explored, and it would be helpful to do more studies with bigger groups of people using advanced techniques. This could help us understand lung problems as a lasting effect of diabetes. Our review did not identify any studies that have investigated the correlation between risks of cardiovascular disease and pulmonary function in individuals with type 2 diabetes mellitus.

**LIMITATION AND FUTURE RECOMMADATIONS**

Diabetes Mellitus is a widely prevalent disease. Till date there is scarce of literature available on the association between cardiovascular disease and pulmonary function. Further studies with large sample and clinical trials are recommended to establish the evidence.

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