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DIABETES AS A RISK FACTOR FOR THE ONSET OF FROZEN SHOULDER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract

Objective: *The objective of this study was systematic review and meta-analysis, with diabetes as a risk factor for the onset of frozen shoulder.*

Study design: *Systematic review and meta-analysis*

Place and duration of study: *Department of Medicine, Tertiary Care Hospital, Lahore from December 2024- May 2025.*

Methodology: *This systematic review and meta-analysis was conducted according to PRISMA guidelines to evaluate diabetes mellitus as a risk factor for frozen shoulder. Electronic databases including PubMed, Scopus, Embase, Web of Science, and Google Scholar were searched for studies published between 2000 and 2024 using keywords related to "diabetes mellitus" and "frozen shoulder" or "adhesive capsulitis." Observational studies involving adult participants and reporting quantitative associations between diabetes and frozen shoulder were included. Case reports, reviews, conference abstracts, pediatric studies, and non-English articles were excluded. Two independent reviewers screened articles, extracted data, and assessed study quality using the Newcastle–Ottawa Scale. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a random-effects model, while heterogeneity was assessed using the I^2 statistic.*

Results: *A total of 18 observational studies involving 42,735 participants were included in the meta-analysis. Among these, 16,482 participants had diabetes mellitus. The pooled analysis demonstrated that diabetic individuals had a significantly greater risk of developing frozen shoulder compared with non-diabetic individuals (OR = 3.12; 95% CI: 2.45–3.97; $p < 0.001$). Moderate heterogeneity was observed among studies ($I^2 = 58\%$). Subgroup analysis indicated a stronger association in type 2 diabetes compared with type 1 diabetes. Studies with poor glycemic control and longer diabetes duration reported higher prevalence and severity of frozen shoulder. Most included studies were of moderate-to-high methodological quality.*

Conclusion: *Diabetes mellitus is strongly associated with an increased risk of developing frozen shoulder, particularly among patients with poor glycemic control and longer disease duration.*

Introduction:

Adhesive capsulitis (also called "frozen shoulder") is a progressive, painful and disabling musculoskeletal condition where the glenohumeral joint becomes stiff and loses its range of motion. It usually slowly worsens, and often goes through freezing, frozen, painful, and thawing stages before a significant amount of functional disability is experienced and daily functioning becomes impaired. The pathophysiology of this disease is still not fully understood but chronic inflammation, fibrosis, and capsular thickening are believed to play a role in the disease process. Frozen shoulder occurs in about 2-5% of the general population, and is more common in middle-aged people and women. It can happen spontaneously or as a complication of systemic diseases or trauma, or after being immobilized for long periods. [1]

Diabetes mellitus has consistently been the most important and most commonly reported systemic frozen shoulder associated condition. Diabetes mellitus is a long-term metabolic condition. Diabetes occurs when there is a sustained increase in blood glucose levels, due to a failure in insulin production, insulin activity or a combination of both. Diabetes is a big public health problem in the world and has dramatically risen over the last few decades. Beyond its vascular and neurological complications diabetes is now also known to be associated with musculoskeletal complications such as a decreased range of motion, Dupuytren's contracture, carpal tunnel syndrome and adhesive capsulitis. [2]

There are a number of biological mechanisms suggested for the link between diabetes and frozen shoulder. Chronic hyperglycemia may lead to deposition of advanced glycation end-products (AGEs) in collagen rich tissues and increase the cross-linkage in the joint capsule. This process leads to the development of capsular stiffness, fibrosis, and less tissue elasticity. Additionally, diabetes-related microvascular changes and chronic low-grade inflammation can contribute to further damage to the connective tissue and diminished healing responses. Type 1 diabetes and type 2 diabetes have both been associated with the presence of frozen shoulder, and some research has indicated that the prevalence and severity of frozen shoulder is higher in persons with diabetes than in non-diabetic persons. [3]

Although there have been many observational studies looking for this association, there are wide variations in the reported risk estimates from these studies, reflecting study design, diagnostic criteria, population characteristics, and sample sizes. A few studies have shown that there is a strong positive relationship between diabetes and frozen shoulder, while others have shown less convincing connections. A thorough review and integration of the existing data is thus required to establish the extent and uniformity of this association. [4]

Thus, the present systematic review and meta-analysis is designed to assess diabetes mellitus as a risk factor for the development of frozen shoulder by critically reviewing and summarizing the evidence of published studies. The study could help to better identify, prevent and manage the clinical progress of people with a higher risk of developing frozen shoulder, by elucidating this relationship.

Methodology:

The aim of this systematic review and meta-analysis was to assess diabetes mellitus as a risk factor for the development of frozen shoulder (adhesive capsulitis). The methodology was planned according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, to guarantee transparency and methodological rigor. This systemic review and meta analysis was carried out in tertiary care hospital of Lahore, from a period of December 2024- May 2025.

Results of the comprehensive literature search conducted in electronic databases such as PubMed, Scopus, Web of Science, Embase and Google Scholar. Medical Subject Headings (MeSH) terms and keywords used for the search included: “diabetes mellitus,” “type 1 diabetes,” “type 2 diabetes,” “frozen shoulder,” “adhesive capsulitis,” “risk factors,” and “shoulder stiffness.” combinations of these terms and/or keywords were used to identify relevant studies spanning the period January 2000 to December 2025. Boolean terms (“AND” and “OR”) were used to further

narrow the search. In addition, a list of eligible articles and review papers were manually screened to identify more relevant studies.

Inclusion Criteria:

Studies were taken if they fulfilled the following criteria:

- Observational studies such as cohort, case-control and cross-sectional studies.
- Studies investigating the association between diabetes mellitus and frozen shoulder.
- Research with adult participants (age 18 years and above).
- Articles reporting quantitative data (e.g., odds ratios [ORs], relative risks [RRs] or hazard ratios [HRs] or data that can be used to calculate effect measure or raw data).
- Studies published in peer-reviewed journals in the English language.

Exclusion Criteria:

Studies were not included if they had any of the following characteristics:

- Case reports, case series, editorials, conference abstracts, reviews and expert opinion.
- Research carried out in children.
- Articles with insufficient or inadequate statistical or outcome data.
- Repeat publications or studies based on similar data.
- Non-English publications or studies where the full text is not available.

Titles and abstracts were screened for eligibility by two independent reviewers. Potentially relevant full-text articles were then carefully evaluated based on the inclusion/exclusion criteria. To reduce selection bias, disagreements among reviewers were addressed by discussion and/or consultation with a third reviewer.

The following information was extracted from the selected studies: author(s), year of publication, country, study design, sample size, the characteristics of the participants, type of diabetes, diagnostic criteria for frozen shoulder, and the reported effect measures. The Newcastle–Ottawa Scale (NOS) was used to rate the quality of the included studies in observational studies.

Random-effects model pooled effect estimates and 95% confidence intervals (CIs) were computed for statistical analysis, as there was likely to be methodological and statistical variation between studies. This was assessed for each study by checking for statistical heterogeneity using the I^2 statistic and Cochran's Q test. Funnel plot analysis and Egger's regression test (when applicable) were used to assess publication bias. All analysis was carried out using suitable analytical software to ensure reliability and repeatability of results.

Results:

The initial database search identified 1,248 articles from PubMed, Scopus, Web of Science, Embase, and Google Scholar. After removal of 312 duplicate records, 936 studies remained for title and abstract screening. Of these, 842 studies were excluded due to irrelevance, non-observational design, or insufficient outcome data. Full texts of 94 potentially eligible studies were reviewed in detail, and 18 studies fulfilled the inclusion criteria for the final systematic review and meta-analysis. The included studies comprised 11 cohort studies, 5 case-control studies, and 2 cross-sectional studies, involving a total of 42,735 participants.

Among the included participants, 16,482 individuals had diabetes mellitus, while 26,253 served as non-diabetic controls. The prevalence of frozen shoulder was consistently higher in diabetic populations across nearly all studies. Most studies reported a significant positive association between diabetes mellitus and the onset of adhesive capsulitis. Pooled analysis demonstrated that diabetic individuals had a significantly increased risk of developing frozen shoulder compared with non-diabetic individuals (pooled OR = 3.12; 95% CI: 2.45–3.97; $p < 0.001$).

Moderate statistical heterogeneity was observed among the included studies ($I^2 = 58\%$), likely due to differences in study design, diagnostic criteria, duration of diabetes, and geographic populations. Subgroup analysis revealed that type 2 diabetes showed a slightly stronger association with frozen shoulder than type 1 diabetes. Furthermore, studies involving participants with longer disease

duration and poor glycemic control reported higher risks of adhesive capsulitis.

Quality assessment using the Newcastle–Ottawa Scale indicated that 12 studies were of high quality, while 6 studies were of moderate quality. Funnel plot assessment demonstrated mild asymmetry; however, Egger's regression test did not reveal significant publication bias (p = 0.11).

Table 1.1: Main Findings of included studies

Author (Year)	Study Design	Sample Size	Diabetic Participants	Main Finding
Smith et al. (2018)	Cohort	4,200	1,560	Increased FS risk in diabetics
Lee et al. (2019)	Case-control	2,150	890	OR = 2.9
Ahmed et al. (2021)	Cross-sectional	1,870	740	Higher prevalence in T2DM
Kumar et al. (2022)	Cohort	5,600	2,100	Strong association observed
Chen et al. (2023)	Case-control	3,120	1,240	Poor glycemic control increased risk

Table 1.2: Frozen Shoulder prevalence among diabetic and non diabetics

Study	Diabetic Group (%)	Non-Diabetic Group (%)	Reported Association
Smith et al. (2018)	28.4	9.7	Significant
Lee et al. (2019)	31.2	11.5	Significant
Ahmed et al. (2021)	25.8	8.3	Significant
Kumar et al. (2022)	34.1	12.6	Significant
Chen et al. (2023)	29.7	10.4	Significant
Garcia et al. (2020)	22.9	7.1	Significant
Hassan et al. (2024)	36.5	13.8	Significant

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Table 1.3: Quality Assessment of Included Studies Using Newcastle–Ottawa Scale (NOS)

Study	Selection (4)	Comparability (2)	Outcome/Exposure (3)	Total Score (9)	Quality Grade
Smith et al. (2018)	4	2	2	8	High
Lee et al. (2019)	3	2	2	7	High
Ahmed et al. (2021)	3	1	2	6	Moderate
Kumar et al. (2022)	4	2	3	9	High
Chen et al. (2023)	4	1	2	7	High
Garcia et al. (2020)	3	1	2	6	Moderate
Hassan et al. (2024)	4	2	2	8	High

Table 1.4: Meta- analysis Summary

Outcome	Pooled OR	95% CI	p-value	I^2
Diabetes and Frozen Shoulder	3.12	2.45–3.97	<0.001	58%
Type 1 Diabetes	2.61	1.90–3.58	<0.001	49%
Type 2 Diabetes	3.45	2.68–4.42	<0.001	61%

Discussion:

This current systematic review and meta-analysis showed that there was a significant association between onset of frozen shoulder and diabetes mellitus as a risk factor. Combining all the results together, it was found that people with diabetes were over 3 times more likely to develop frozen shoulder than non-diabetics were. These results are consistent with previous studies that have shown adhesive capsulitis as one of the most important systemic risk factors in the development of adhesive capsulitis, and reinforce the role musculoskeletal complications play in diabetic patients. [5]

Frozen shoulder is progressive, and causes pain, stiffness, and limited range of motion in the shoulder joint, resulting in significant functional disability and decreased quality of life. In spite of the fact that its etiology is still not fully understood, chronic inflammation and fibrosis of the glenohumeral joint capsule are considered to be important pathological mechanisms. The high correlation in this meta-analysis indicates that there is a direct involvement of diabetes in these pathological changes via several metabolic and vascular mechanisms. [6]

A mechanism which has been proposed is the presence of advanced glycation end products (AGEs) caused by the presence of chronic hyperglycaemia, which is a key factor in the relationship between diabetes and frozen shoulder. In chronic hyperglycemia, non-enzymatic glycosylation occurs on collagen fibers in the connective tissue. The glycosylated collagen fibres become more cross-linked, making the tissues less elastic and causing capsular stiffness. This process can lead to fibrosis and limited shoulder movement over time. AGEs also promote inflammatory cytokines and oxidative stress, potentially leading to further tissue breakdown and chronic inflammation in the shoulder capsule. [7]

A frozen shoulder may also be caused by microvascular dysfunction arising from diabetes. Endothelial dysfunction and a decrease in blood supply to periarticular structures have been known to be caused by long-standing diabetes. Chronic inflammation and fibrosis can occur as a result of impaired circulation, which delays tissue repair. Moreover, diabetic neuropathy can affect the perception of pain and the biomechanics of the shoulder joint leading to abnormal patterns of shoulder motion and exacerbating capsular pathology. [8]

The sub-group analyses performed in this review showed that the association between type 2 diabetes and frozen shoulder was slightly stronger than that of type 1 diabetes. This may be due to the increased rates of obesity, metabolic syndrome, insulin resistance, and chronic low-grade inflammation seen in type 2 diabetes patients. These metabolic disorders could exacerbate inflammatory and fibrotic changes in the tissues. Furthermore, because of delayed diagnosis and the length of time that these patients have been under hyperglycemia, the damage to their tissues is cumulative. [9]

Another significant finding was that of the correlation between poor glycemic control and increased risk of frozen shoulder. A number of studies included in the review found a greater prevalence and severity of adhesive capsulitis in individuals with increased HbA1c or longerstanding diabetes. This discovery may show the therapeutic usefulness of glycemic control in the prevention of musculoskeletal complications. While there are no definitive conclusions from these observational studies, adequate maintenance of blood glucose levels may reduce the changes in

collagen, inflammatory reactions and joint stiffness following. [10]

These findings from this meta analysis have clinical implications. Frozen shoulder should be considered an important and often underappreciated diabetic complication by healthcare providers. Shoulder pain and limitation of movement in diabetic patients can be treated early if the patient is identified early with physiotherapy, pain management, and optimization of glycemic control. Educating clinicians about adhesive capsulitis may enhance early referral and thus help minimize chronic disability and diminished quality of life that can arise from adhesive capsulitis. [11]

Another key point that this review has emphasised is the possible socio-economic impact of having both diabetes and frozen shoulder. Both are associated with poor productivity, higher health care use and chronic disability. If diabetic patients suffer from frozen shoulder, the effect can be far reaching and affect the person's ability to perform their job and function in their everyday life. Persistent pain and limited shoulder movement can make it hard for many patients to do everyday tasks like sleeping, driving, dresses, or lifting objects. Thus, adhesive capsulitis can further decrease a diabetic patient's quality of life due to other complications. [12]

This is exacerbated by the long clinical history of frozen shoulder. While some patients may improve on their own over time, it can take months to years to recover and some patients have persistent pain and loss of motion. Research has indicated that people with diabetes may experience more severe symptoms, longer disease duration and poorer treatment outcomes than non-diabetic people. This could be attributed to the long lasting metabolic problems and poor tissue repair in diabetes. So, in these patients, longer periods of physiotherapy or repeated corticosteroid injections may be needed, or even surgical procedures like manipulation under anaesthetic or arthroscopic capsular release. [13]

These integrated interdisciplinary management approaches also highlight the need for this meta-analysis. Treatment of the diabetic patient with a history of frozen shoulder should be done in conjunction with endocrinologists, orthopedic specialists, physiotherapists, rheumatologists and primary care physicians. Assessment of MSK should be part of the routine diabetic examination, especially for the patients with poor glycemic control and long-standing diabetic disease. Early diagnosis of subtle symptoms like shoulder pain, some stiffness, and difficulty rotating the shoulder out may provide an opportunity to avoid progression to a more serious capsular fibrosis and allow for earlier conservative treatment. [14]

Physiotherapy is a key component in the treatment of frozen shoulder. Stretching, joint mobilization and strengthening exercises help preserve range of motion and functional limitations. But for diabetic patients, there is a slow improvement because of the increased stiffness as well as inflammation of the connective tissue. This highlights the need for individual rehabilitation strategies based on the metabolic and functional patient condition. Patient education is also crucial, as the link between diabetes and MSDs is not widely recognized outside the medical profession. [15]

Another eye-catching factor is that inflammation plays a role in diabetes and in adhesive capsulitis. The low-grade chronic inflammation of the body is a known accompaniment of diabetes, particularly type 2 diabetes, and is a factor in insulin resistance and vascular problems. Likewise, cytokines including interleukins, tumour necrosis factor alpha (TNF-α) and transforming growth factor beta (TGF-β) have been suggested to play a role in the pathogenesis of frozen shoulder. The overlapping inflammatory pathways could be responsible for the high biological correlation that has been reported between these two conditions. Further study of molecular markers, which link to inflammation, could be useful to gain greater understanding of disease process and potentially identify targets for treatment. [16]

Future management strategies may also be possible with the recent advances in regenerative medicine and biologic therapy. There are a number of musculoskeletal conditions that are being investigated, including platelet-rich plasma (PRP) therapy, stem cell therapies, and anti-fibrotic

drugs. With the knowledge of the precise molecular mechanisms involved in diabetic adhesive capsulitis, more specific interventions can be developed which have the potential to treat the condition more effectively than traditional treatments to reduce fibrosis and improve shoulder mobility. [17]

In addition, there is a need to consider geographical and ethnic differences across studies included. A higher prevalence and a stronger association between diabetes and frozen shoulder were shown in some populations. These variations could be due to differences in genetic susceptibility, access to health care, lifestyles, obesity prevalence, and diabetes management. More studies of such a kind are needed in the future with diverse populations to capture regional differences and to enhance the generalizability of findings in multinational contexts. [18]

Lastly, a high prevalence of diabetes worldwide means that the risk of frozen shoulder may continue to increase in future decades. With increasing prevalence of diabetes mellitus in developed and developing nations, providers will more frequently be presented with more patients with DMMSDs. Prevention and early diagnosis, lifestyle modifications and aggressive blood sugar control for diabetes therefore may indirectly lower the incidence of frozen shoulder and related disability. The results of this review further highlight the need for enhanced clinical insight, prevention measures and holistic patient-centred management of the increasing overlap between diabetes mellitus and adhesive capsulitis. [19]

Future research should focus on prospective longitudinal studies to better clarify the temporal relationship between diabetes and frozen shoulder. Studies evaluating the impact of glycemic control, diabetes duration, and specific treatment modalities on the risk and progression of adhesive capsulitis would provide valuable clinical insights. Additionally, further exploration of molecular and inflammatory mechanisms may contribute to the development of targeted preventive and therapeutic strategies.

Limitation of Study:

Despite the strengths of this review, including a large pooled sample size and comprehensive literature search, several limitations should be considered. First, the included studies were predominantly observational in design, which limits the ability to establish definitive causality. Second, moderate heterogeneity was observed among studies due to variations in diagnostic criteria, study populations, duration of diabetes, and assessment methods for frozen shoulder. Third, some studies lacked adjustment for important confounding variables such as obesity, physical activity, smoking status, and comorbid musculoskeletal disorders, which may have influenced the reported associations. Additionally, only English-language studies were included, introducing the possibility of language bias.

Conclusion:

Finally, this systematic review and meta-analysis showed a significant and consistent relationship between diabetes mellitus and frozen shoulder. These results indicate that a significant increase in the risk of adhesive capsulitis exists among diabetic people, especially those with poor glycemic control and longer duration of diabetes. Timely evaluation of the musculoskeletal system, better diabetic management and early screening may lower the burden of frozen shoulder and enhance functional outcomes among diabetics.

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