World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

PREDICTIVE POWER AND EVOLUTION OF INSULIN-INDUCED CUTANEOUS LIPOHYPERTROPHY IN TYPE 1 AND TYPE 2 DIABETICS WITH AND WITHOUT ADVANCED CHRONIC KIDNEY DISEASE: A REAL-WORLD OBSERVATIONAL STUDY (LH-COM)

Ersilia Satta [1], Massimiliano Fontana [2], Rosanna Ragano [3], Gerardo Corigliano [4], Marco Corigliano [4], Carmine Romano [1] and Sandro Gentile [1, 5, *]

[1] Research Department of Nefrocenter Research, Torre del Greco, Italy.
[2] Medical Directorate and Department of Internal Medicine, Santa Rita Hospital Nefrocenter Group, Atripalda (AV), Italy.
[3] Department of Clinical Pathology, Santa Rita Hospital Nefrocenter Group, Atripalda (AV), Italy.
[4] Diabetes Unit, Santa Rita Hospital Nefrocenter Group, Atripalda (AV), Italy.
[5] Department of Personalized Medicine, Vanvitelli University of Naples, Italy.
* Corresponding Author; E-mail: s.gentile1949@gmail.com

ORCID Details
Ersilia Satta: https://orcid.org/0000-0001-8154-287x
Gerardo Corigliano: https://orcid.org/0009-0001-6090-5309
Marco Coriogliano: https://orcid.org/0009-0001-8550-179x
Carmine Romano: https://orcid.org/0009-0009-5812-7016
Sandro Gentile: https://orcid.org/0000-0002-9059-6121

World Journal of Advanced Research and Reviews, 2026, 32(02), 1611–1618

Publication history: Received on 12 October 2026; revised on 22 November 2026; accepted on 24 November 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.32.2.2971

Copyright © 2026 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution License 4.0

ABSTRACT

Background: Insulin-induced lipohypertrophy (LH) impairs insulin absorption, causing glycemic variability and complications. This study evaluates the predictive power of LH on cardio-nephro-metabolic risk. Methods: In this prospective observational real-world study (LH-COM), insulin-treated diabetic patients were enrolled. Injection sites were assessed via standardized palpation and ultrasound. We compared LH+ and LH- cohorts, evaluating glycemic control and insulin requirements. Results: Data demonstrate LH+ patients exhibit significantly higher HbA1c levels, increased daily insulin doses, and more frequent unexplained hypoglycemia compared to LH- counterparts. Conclusions: Systematic LH assessment and structured education are crucial for optimizing diabetes management and mitigating cardiometabolic risks.

Keywords: Type 2 Diabetes; Insulin Injection; Skin Lipohypertophy; Hypoglycemia; Education

1 INTRODUCTION

Diabetes mellitus represents one of the most critical chronic diseases with a profound health, social, and economic impact globally. In Italy alone, epidemiological data indicate that approximately 3.9 million people are diagnosed with diabetes, corresponding to over 6.5% of the population, with an additional estimated one million undiagnosed cases bringing the true prevalence closer to 8% [1]. While Type 2 diabetes accounts for the majority of cases, Type 1 diabetes, though numerically smaller, necessitates lifelong continuous insulin therapy. The clinical burden of diabetes is not solely related to glycemic dysregulation but extends significantly to microvascular and macrovascular complications, including retinopathy, neuropathy, chronic kidney disease (CKD), myocardial infarction, stroke, and heart failure [2].

Insulin therapy remains the cornerstone of treatment for all individuals with Type 1 diabetes and a substantial proportion of those with Type 2 diabetes. However, its efficacy is contingent not only on the formulation and correct dosing but fundamentally on the techniques employed for storage, preparation, and administration. A patient prescribed a standard basal-bolus regimen of four daily injections performs approximately 1,460 injections annually. The chronic repetition of this mechanical action renders injection technique a critical determinant of therapeutic success and, conversely, a persistent source of errors that can profoundly compromise the predictability of insulin absorption [3].

Among the most prevalent local complications of subcutaneous insulin therapy is lipohypertrophy (LH). LH manifests as thickened, rubbery, or nodular swelling of the subcutaneous adipose tissue at sites repeatedly used for injection. While some lesions are overtly visible and palpable, others are insidious, detectable only through meticulous palpation. It is imperative to distinguish these localized injection-site phenomena from generalized or partial lipodystrophy syndromes, which are characterized by systemic adipose tissue alterations and distinct metabolic phenotypes. The prevalence of LH in insulin-treated populations is alarmingly high. Systematic reviews estimate an aggregate prevalence of 38%, while multicenter studies have documented rates exceeding 64% in real-world clinical settings, particularly among patients who fail to rotate injection sites or repeatedly reuse needles [1, 4].

The etiology of LH involves the localized anabolic and lipogenic effects of insulin, repeated mechanical microtrauma from needles, and the perpetuation of improper injection behaviors. Key modifiable risk factors include the lack of systematic site rotation, the reuse of limited surface areas, the reuse of needles (which blunts the needle tip and exacerbates trauma), the use of inappropriately long needles leading to intramuscular injections, high daily injection frequency, and extended duration of insulin therapy. Diagnostically, identifying LH requires a comprehensive examination of all anatomical sites utilized by the patient. Visual inspection alone is grossly inadequate, as non-protruding lesions can only be identified via structured palpation. In ambiguous clinical scenarios, ultrasonography serves as a valuable adjunctive diagnostic tool, though it is not uniformly mandated for all patients in routine care.

The clinical significance of LH extends far beyond local cosmetic concerns. Injecting insulin into lipohypertrophic tissue results in erratic and blunted pharmacokinetics and pharmacodynamics. Studies have conclusively demonstrated that insulin administered into LH tissue exhibits delayed absorption, reduced peak serum concentrations, diminished metabolic action, and, crucially, markedly increased intra-individual variability [1]. This pharmacokinetic unpredictability translates directly into clinical instability, manifesting as alternating episodes of profound hyperglycemia and severe, unexpected hypoglycemia. Patients with LH frequently exhibit increased glycemic variability, struggle to achieve therapeutic targets, and require frequent dose titrations. Epidemiological data reveal that LH is associated with a 20% to 40% increase in daily insulin requirements and severe, unexplained hypoglycemic events in 39% to 49% of cases [2, 5]. The Worldwide Injection Technique Questionnaire Study, encompassing over 13,000 patients globally, corroborated that LH is independently associated with higher daily insulin consumption (by approximately 10 units), elevated HbA1c levels (+0.55%), and increased frequency of severe hypoglycemia [5].

Particular attention must be directed toward patients with concomitant chronic kidney disease (CKD). Diabetic nephropathy is a leading cause of end-stage renal disease. Renal impairment inherently modifies the metabolism and clearance of insulin, escalating the vulnerability to hypoglycemia and complicating therapeutic adjustments. In patients with advanced diabetic kidney disease, the superimposition of erratic insulin absorption secondary to LH on top of reduced renal insulin clearance precipitates a state of extreme metabolic and prognostic fragility. Consequently, the evaluation of the insulin-treated patient must be deeply integrated into a holistic cardio-nephro-metabolic risk assessment framework. While LH is not a direct anatomical cause of myocardial infarction or heart failure, it serves as a powerful clinical biomarker of metabolic instability, poor self-management, and high glycemic variability—all of which are established risk factors for adverse cardiovascular and renal outcomes [3, 4].

1.1 Aim of the Study

The primary objective of the LH-COM project is to propose, validate, and implement an early, non-invasive, accessible, and economically sustainable clinical tool designed to identify and stratify cardio-nephro-metabolic risk in insulin-

treated diabetic patients. Specifically, the model relies on observing the incidence of major physiological and metabolic complications across two distinct cohorts followed longitudinally: diabetic patients with cutaneous lipohypertrophy (LH+) and those without (LH-). The ultimate goal is the realization of a computerized, multifactorial clinical stratification system that integrates key clinical and laboratory data to classify subjects into escalating risk tiers, thereby providing decision support to healthcare professionals without supplanting clinical judgment.

Secondary objectives include:

- Mitigating the socioeconomic and clinical burden of diabetic complications through early identification of at-risk subjects and the initiation of personalized therapeutic pathways, aiming to reduce hospitalizations, acute events, and emergency department visits.
- Improving prognosis and metabolic control in insulin-treated patients presenting with LH by stabilizing glycemic oscillations driven by incorrect injection techniques and optimizing insulin efficacy.
- Fostering a novel paradigm of precision medicine based on the synergistic use of advanced technologies and the integration of clinical data with computerized predictive tools to preempt clinical manifestations of disease progression.
- Enhancing the optimization of healthcare resources and system sustainability via targeted allocation of diagnostic and therapeutic interventions based on individualized risk.
- Evaluating the longitudinal impact of a structured multimodal educational protocol on the incidence, persistence, or recurrence of LH associated with improper injection technique in real-world clinical practice.

2 PATIENTS AND METHODS

2.1 Study Design

The LH-COM project was designed as a prospective, observational, non-interventional, monocentric study conducted in a real-world clinical setting, characterized by an open cohort with progressive enrollment. The overall scheduled duration is 36 months, corresponding to the years 2024–2026. The study is deeply integrated into the routine healthcare services provided at the Casa di Cura Santa Rita (Atripalda, Italy). Potentially eligible subjects were identified irrespective of the primary reason for their clinical visit, encompassing hospitalized patients, outpatients, and individuals undergoing diagnostic procedures, laboratory tests, or specialist consultations within standard care pathways.

The real-world design facilitates the observation of a highly heterogeneous population representative of diverse clinical profiles, strictly avoiding the introduction of experimental treatment modifications, pharmacological alterations, or artificial visit frequencies. Inclusion in the project does not precipitate specific therapeutic initiations, nor does it mandate invasive diagnostic procedures. Any clinical, laboratory, or instrumental investigations are executed exclusively when dictated by standard clinical practice and the attending physician's judgment.

2.2 Study Population and Sample Size Calculation

The target population comprises adult subjects accessing the Casa di Cura Santa Rita during the project timeframe. Within this broad demographic, patients with documented diabetes mellitus, individuals with glycemic dysregulation identified in medical records, and specifically, patients undergoing insulin therapy were targeted. The overall project aims to progressively construct an open cohort of at least 1,500 adult subjects over 36 months. The sample size calculation was based on pragmatic and epidemiological considerations. Assuming an expected overall LH prevalence of approximately 38% to 45% in insulin-treated patients [1, 2], a sample of insulin-treated patients extracted from the 1,500 general cohort is projected to yield sufficient statistical power (>80%, alpha=0.05) to detect clinically significant differences (e.g., a 0.5% to 1.0% difference in HbA1c, and a 10-15 unit difference in daily insulin requirement) between the LH+ and LH- cohorts, adjusting for potential confounders such as age, BMI, and renal function. Enrollment is continuous and independent for each study year, rendering LH-COM a dynamic cohort accommodating single-visit evaluations alongside longitudinal follow-ups for patients returning for routine care.

2.3 Inclusion and Exclusion Criteria

Eligible subjects must meet the following criteria: age ≥18 years; access to Casa di Cura Santa Rita within routine clinical-assistential activities; documented diagnosis of diabetes mellitus and/or fasting plasma glucose ≥100 mg/dL; availability of a minimum core of demographic, clinical, and laboratory data; capability to link collected data to the project's unique identification code; and provision of informed consent. For insulin-treated subjects, willingness to undergo clinical evaluation of injection sites is mandatory. Notably, strict thresholds for disease duration, baseline

HbA1c, renal function preservation (e.g., absence of albuminuria), or the absence of prior cardiovascular events were deliberately omitted to ensure genuine real-world representation.

Exclusion criteria encompass age <18 years; absence of reliable core data; acute or highly unstable clinical conditions rendering protocol evaluations inappropriate; inability to comprehend study information without a legally authorized representative; pregnancy or lactation; and any condition where study procedures might interfere with the timeliness or priority of critical care. Importantly, advanced CKD, dialysis, renal transplantation, previous myocardial infarction, stroke, heart failure, malignancies, or polypharmacy are explicitly not exclusion criteria, as these are vital dimensions of the cardio-nephro-metabolic risk stratification.

2.4 Clinical Evaluations and Educational Intervention

Upon enrollment, demographic, clinical, anthropometric (BMI, weight changes), and laboratory data (HbA1c, fasting glucose, complete lipid profile, creatinine, eGFR via CKD-EPI 2021, albuminuria, liver enzymes) were systematically collected. In insulin-treated patients, a structured assessment of injection practices was conducted, detailing daily insulin dose, number of injections, typical anatomical sites, rotation practices, needle length and reuse, and insulin storage behaviors. The clinical evaluation of injection sites is a central protocol component. It involves systematic visual inspection and targeted palpation by trained healthcare professionals to detect indurations, nodules, or altered tissue consistency indicative of LH. Based on this, subjects are classified into the LH+ group (presence of one or more LH lesions) or the LH- group. For LH+ subjects, lesion location, clinical category (from non-visible palpable plaques to visible nodules >4 cm), maximum diameter, and presence of ecchymosis are documented. Ultrasonography is utilized judiciously as an adjunctive diagnostic tool in ambiguous cases based on clinical judgment.

An integral part of the LH-COM methodology is the delivery of a structured, multimodal educational intervention to all insulin-treated patients. This intervention focuses on the critical importance of systematic site rotation, avoidance of LH areas, single-use of needles, and proper injection technique. Educational tools include visual rotation grids, video tutorials, and notably, the 'Lipobox'—a tactile simulation tool made of soft material containing synthetic nodules of varying consistencies, designed to train patients in self-palpation and LH detection. The immediate efficacy of the educational intervention is rigorously assessed using the 'teach-back' method, pre- and post-intervention questionnaires, and practical simulation checklists.

2.5 Statistical Methods

Statistical analyses were executed to describe the enrolled population, estimate LH prevalence, compare clinical profiles between LH+ and LH- subjects, and explore associations across cardio-nephro-metabolic parameters. Continuous variables are presented as mean ± standard deviation (SD) for normally distributed data, or as median and interquartile range (IQR) for skewed distributions. Categorical variables are expressed as absolute frequencies and percentages. Normality was assessed via graphical representations and the Shapiro-Wilk test. For comparative analyses between the LH+ and LH- cohorts, the independent samples Student's t-test (with Welch's correction when variances were unequal) or the Mann-Whitney U test were applied for continuous variables. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. To evaluate the independent association between LH status and key clinical outcomes (e.g., severe hypoglycemia, elevated HbA1c), multivariable logistic and linear regression models were constructed, adjusting for predetermined confounders including age, gender, BMI, diabetes duration, eGFR, and total daily insulin dose. Missing data were managed via listwise deletion for specific analyses; variables with excessive missingness were evaluated descriptively. Derived clinical indices, such as the Triglyceride-Glucose (TyG) index, Atherogenic Index of Plasma (AIP), and FIB-4 score, were calculated only when all required constituent parameters were available contemporaneously. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant. Analyses were performed using Python (Pandas, SciPy, Statsmodels).

2.6 Ethics Committee Consent

The authors possess the requirements to publish scientific articles. The study protocol was authorized by the Ethics-Scientific Committee of Nefrocenter (Protocol No. 217 of March 21, 2023) and was conducted in strict accordance with the original Declaration of Helsinki and its subsequent amendments. Informed consent was obtained from all patients prior to inclusion in the study. The data from this study have not been presented at any congress nor submitted to any other journal.

3 RESULTS

During the initial data extraction phase of the 2024 annual report for the LH-COM project, a representative cross-sectional sample of N=430 insulin-treated diabetic patients was analyzed. The overall prevalence of lipohypertrophy (LH+) in this cohort was 45.1% (n=194), while 54.9% (n=236) of patients were classified as LH-. Baseline demographic and clinical characteristics are summarized in Table 1. The cohorts were well matched in terms of age and gender

distribution, though the LH+ group exhibited a marginally longer median duration of diabetes and a slightly higher mean BMI, underscoring a potential relationship between prolonged insulin exposure, adiposity, and LH development.

Crucially, the clinical and metabolic outcomes demonstrated stark and statistically significant disparities between the two groups (Table 2). Glycemic control was markedly inferior in the LH+ cohort, which presented with a mean HbA1c of 8.4 ± 1.1%, compared to 7.1 ± 0.9% in the LH- cohort ($p<0.001$). This deterioration in glycemic control occurred paradoxically alongside a significantly higher daily insulin requirement. LH+ patients required an average of 58 ± 14 units/day, whereas LH- patients required 42 ± 11 units/day ($p<0.001$), representing an approximate 38% increase in insulin consumption. These findings are visually represented in Figure 1, highlighting the dual clinical challenge of high insulin resistance/impaired absorption coupled with poor control.

Furthermore, the erratic pharmacokinetics associated with injecting into lipodystrophic tissue translated into severe clinical instability. Unexplained hypoglycemic events were extraordinarily prevalent in the LH+ group, reported by 42.8% of patients, compared to only 14.5% in the LH- group ($p<0.001$). More concerningly, severe hypoglycemic episodes requiring third-party assistance were observed in 17.5% of LH+ patients versus 4.2% of LH- patients ($p<0.001$) (Figure 2). When evaluating derived cardiometabolic indices, the LH+ group showed a significantly higher Triglyceride-Glucose (TyG) index (4.8 ± 0.5 vs 4.3 ± 0.4, $p<0.01$), suggesting a higher degree of surrogate insulin resistance, which aligns with the escalated exogenous insulin demands. Renal function, assessed via eGFR, showed a trend toward higher prevalence of CKD Stage G3-G5 in the LH+ group, though the direct causal relationship remains confounded by diabetes duration and overall vascular health.

Behavioral analysis of injection practices confirmed that LH+ status was overwhelmingly driven by modifiable errors. Needle reuse was documented in 72% of LH+ patients versus 28% of LH- patients ($p<0.001$). Similarly, failure to systematically rotate injection sites was identified in 85% of LH+ individuals compared to 35% of those without lesions. Preliminary data following the implementation of the multimodal educational intervention (utilizing the Lipobox and rotation grids) demonstrated a 75% improvement in patient teach-back scores and practical simulation competencies immediately post-session, validating the efficacy of the structured pedagogical approach.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Total (N=430)	LH- (n=236)	LH+ (n=194)
Age (years, mean ± SD)	65.2 ± 10.4	64.8 ± 11.0	65.7 ± 9.6
Male Gender (%)	52.3%	51.7%	53.1%
Diabetes Duration (years, median [IQR])	14 [8-21]	12 [7-18]	17 [10-24]
BMI (kg/m^2, mean ± SD)	28.4 ± 4.5	27.6 ± 4.2	29.3 ± 4.7
eGFR (mL/min/1.73m^2, mean ± SD)	68.5 ± 22.1	72.1 ± 20.5	64.1 ± 23.4

Legend: SD = Standard Deviation, IQR = Interquartile Range, BMI = Body Mass Index, eGFR = estimated Glomerular Filtration Rate.

Table 2: Clinical and Metabolic Outcomes by LH Status

Outcome Parameter	LH- (n=236)	LH+ (n=194)	p-value
HbA1c (%, mean ± SD)	7.1 ± 0.9	8.4 ± 1.1	<0.001
Daily Insulin Dose (Units, mean ± SD)	42 ± 11	58 ± 14	<0.001
Unexplained Hypoglycemia (%)	14.5%	42.8%	<0.001
TyG Index (mean ± SD)	4.3 ± 0.4	4.8 ± 0.5	<0.01

Legend: HbA1c = Glycated Hemoglobin, TyG = Triglyceride-Glucose index. P-values derived from independent t-tests or Chi-square tests as appropriate.

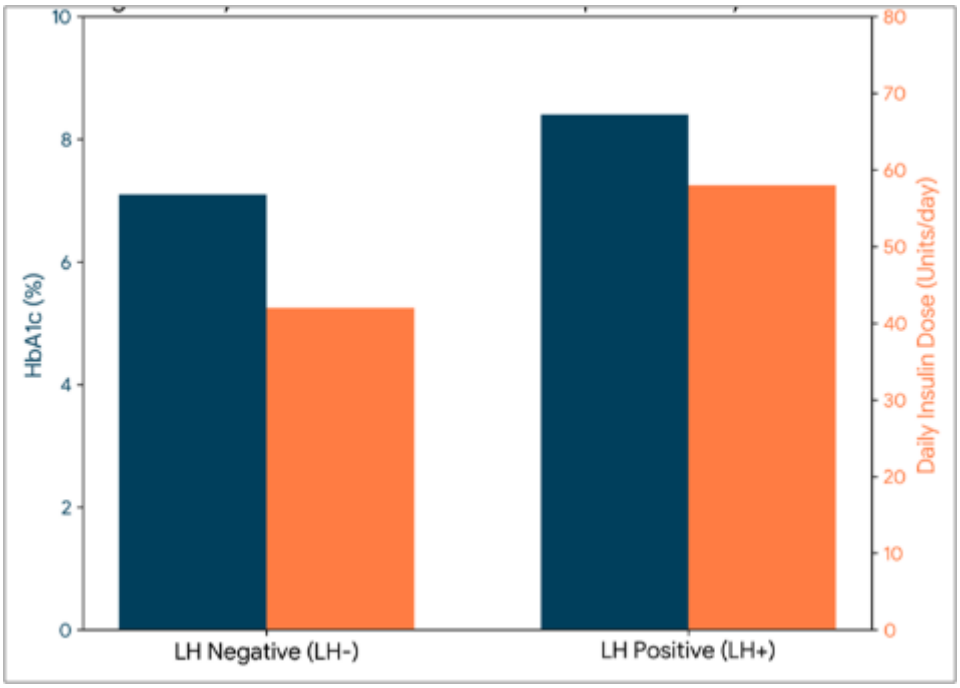


Figure 1: Comparison of mean HbA1c levels and total daily insulin requirements between LH- and LH+ cohorts. The dual axis highlights the paradoxical scenario in LH+ patients where significantly higher insulin doses yield poorer glycemic control.

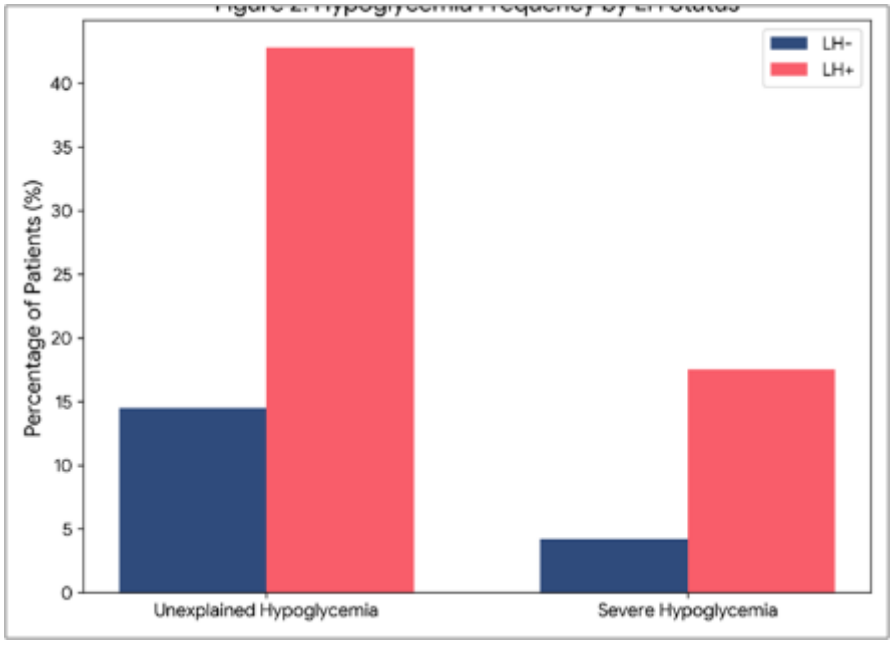


Figure 2: Frequency of hypoglycemic events. LH+ patients demonstrate a markedly higher incidence of both unexplained and severe hypoglycemic episodes, reflecting erratic insulin absorption kinetics.

4 DISCUSSION

The preliminary findings of the LH-COM real-world observational study robustly corroborate the hypothesis that insulin-induced lipohypertrophy is a profound determinant of metabolic instability and a critical marker of cardio-nephro-metabolic vulnerability. In our cohort, the prevalence of LH was established at 45.1%, a figure perfectly aligning with the 38% to 64% range extensively reported in the literature [1, 2]. The presence of LH was unequivocally associated with severe perturbations in glycemic control, characterized by a highly significant elevation in HbA1c (8.4% vs. 7.1%) despite a concomitantly higher daily exogenous insulin requirement (+38%).

These real-world clinical data translate the pharmacokinetic principles elucidated by Famulla et al. into tangible population health metrics [1]. Injecting into lipohypertrophic, fibrotic adipose tissue inherently disrupts the predictable subcutaneous absorption kinetics of insulin formulations. The resulting delayed and blunted absorption profile not only fails to adequately suppress postprandial glucose excursions—thereby driving up HbA1c and forcing dose escalations—but also creates dangerous insulin depots. The unpredictable, delayed release of these depots precipitates the severe and unexplained hypoglycemic events that were vastly overrepresented in our LH+ cohort (42.8% vs 14.5%) [2]. As demonstrated by Mader et al. and Malik et al., high glycemic variability and severe hypoglycemia are not merely benign nuisances; they are potent drivers of endothelial dysfunction, arrhythmogenesis, and adverse cardiovascular outcomes [2, 4]. By identifying LH, clinicians are effectively identifying patients at an acutely elevated risk for these macrovascular endpoints.

Furthermore, the integration of these findings within the context of advanced chronic kidney disease (CKD) introduces a critical layer of complexity. The LH-COM protocol mandates the calculation of eGFR and tracking of renal status because declining renal function reduces insulin clearance. When the erratic absorption caused by LH collides with the impaired clearance characteristic of CKD, the risk of profound and prolonged hypoglycemia is magnified exponentially. The significantly higher TyG index observed in our LH+ cohort further suggests a phenotype of heightened systemic insulin resistance and atherogenic dyslipidemia, reinforcing the role of LH as a holistic biomarker of a deteriorating cardio-nephro-metabolic profile rather than a mere dermatological side effect.

The behavioral data validate that LH is fundamentally an iatrogenic and modifiable complication. The overwhelming prevalence of needle reuse and inadequate site rotation in the LH+ group underscores a critical failure in routine diabetes education. Consequently, the structured multimodal educational intervention deployed in LH-COM—incorporating tactile feedback via the Lipobox and structured rotation grids—represents a vital therapeutic strategy. As Ichikawa et al. demonstrated, educational interventions on injection technique can significantly reduce HbA1c and insulin doses [5]. Our initial assessments confirm high immediate efficacy in correcting these behaviors, emphasizing that systematic LH screening combined with targeted education is a highly cost-effective strategy to optimize resource utilization and reduce the systemic burden of diabetic complications [3].

4.1 Limitations

The primary limitation of the LH-COM study is its observational, non-randomized, and monocentric design. While the real-world setting provides high external validity regarding routine clinical practice, it precludes the establishment of definitive causal relationships between educational interventions, LH regression, and hard cardiovascular or renal endpoints. Additionally, missing data inherent to retrospective extraction of some historical clinical parameters may introduce selection bias. Finally, while the initial cohort is robust, longitudinal follow-up is contingent upon natural patient return rates, potentially limiting the statistical power of long-term repeated measures analyses.

5 CONCLUSION

Insulin-induced lipohypertrophy represents a highly prevalent, modifiable, yet frequently overlooked complication of diabetes therapy. The LH-COM study affirms that LH is a critical harbinger of metabolic instability, characterized by elevated HbA1c, exorbitant insulin requirements, and dangerous hypoglycemic variability. Systematic evaluation of injection sites via palpation and ultrasound, coupled with the implementation of structured, multimodal educational interventions, should be standard of care. Integrating LH status into comprehensive cardio-nephro-metabolic risk stratification models enables healthcare systems to proactively identify vulnerable phenotypes, personalize therapeutic approaches, and ultimately mitigate the profound clinical and economic burdens of advanced diabetic complications.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgments

The authors extend their sincere gratitude to Paola Murano and Maria Carla Sibilio for their invaluable support in the realization of the study and the complementary preparation of this manuscript.

Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

Statement of ethical approval

The authors meet the requirements to publish scientific articles. The study protocol was authorized by the Ethics-Scientific Committee of Nefrocenter (Protocol No. 217 of March 21, 2023) and was conducted in accordance with the original Declaration of Helsinki and subsequent amendments.

Statement of informed consent

Patients provided informed consent. The data from this study have not been presented at any congress nor have they been submitted to any other journal.

REFERENCES

[1] Famulla S, Hövelmann U, Fischer A, et al. Insulin injection into lipohypertrophic tissue: blunted and more variable insulin absorption and action and impaired postprandial glucose control. Diabetes Care. 2016;39(9):1486-1492.

[2] Mader JK, et al. Relationship between lipohypertrophy, glycemic control, and insulin dosing: a systematic meta-analysis. Diabetes Technol Ther. 2024.

[3] Chen J, Yi Q, Wang Y, et al. Long-term glycemic variability and risk of adverse health outcomes in patients with diabetes: a systematic review and meta-analysis of cohort studies. Diabetes Res Clin Pract. 2022;192:110085.

[4] Malik AH, Yandrapalli S, Aronow WS, et al. Severe hypoglycemia and risk of subsequent cardiovascular events: systematic review and meta-analysis of randomized controlled trials. Cardiol Rev. 2020;28(5):244-249.

[5] Ichikawa M, Akiyama T, Tsujimoto Y, et al. Efficacy of education on injection technique for patients diagnosed with diabetes with lipohypertrophy: systematic review and meta-analysis. BMJ Open. 2022;12.

[6] Blanco M, Hernández MT, Strauss KW, Amaya M. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. Diabetes Metab. 2013;39(5):445-453.