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Lipohypertrophy

What's new? Part I

Lipohypertrophy (LH) is a common cutaneous complication in people with diabetes who administer insulin, either by injections or by continuous subcutaneous insulin infusion (CSII). It is characterised by a localised increase in subcutaneous adipose tissue at injection sites.1 This condition results from the combination of insulin's lipogenic action and repeated tissue trauma due to ongoing injections in the same area.2 Key risk factors identified for the development of LH include duration of insulin therapy, failure to rotate injection sites, needle reuse, and the number of daily injections. (2, 4).

Needle reuse, in particular, has proven to be a significant factor, as needles lose lubrication and sharpness, causing greater tissue damage and promoting LH formation (1, 4). Macroscopically, LH presents as a lump or induration of the tissue, often easier to palpate than to see.1 Microscopically, on biopsy there is an increase in both the number and size of adipocytes ***(image 1)***.

Insulin therapy is fundamental for many PwD, especially those with type 1 diabetes mellitus and a growing number with type 2 diabetes mellitus, to achieve glycaemic targets and prevent long-term complications. However, insulin therapy is not without challenges and complications, one of the most common and clinically significant being LH (1, 2).

Despite its high prevalence (a meta-analysis of 12,493 subjects from 26 randomised controlled trials) reporting an average LH prevalence of up to 38% among insulin-treated subjects5 and its known impact on insulin absorption, LH is often underestimated and underdiagnosed in clinical practice (2). Its presence not only affects appearance and comfort but—more critically—compromises insulin pharmacokinetics, leading to erratic and unpredictable drug absorption (1, 3).

This inconsistent insulin absorption from LH-affected sites has profound implications for diabetes management. It has been shown to contribute to greater glycaemic variability, increased daily insulin requirements to reach therapeutic goals, and a higher frequency of hypoglycaemic episodes, including those of unexplained nature.1,3,4 Traditionally, LH detection has relied on clinical palpation—a method shown to be less sensitive and specific compared with more advanced imaging techniques such as ultrasound (2).

GLYCAEMIC VARIABILITY

The relationship between LH and glycaemic variability is critical. LH contributes to increased glycaemic variability. Several studies have shown that LH tissue leads to extremely high variability, primarily due to greater postprandial glucose excursions compa- »

INSULIN THERAPY IS ESSENTIAL FOR MANY PEOPLE WITH DIABETES (PWD), ESPECIALLY THOSE WITH TYPE 1 DIABETES MELLITUS AND A GROWING NUMBER OF PWD WITH TYPE 2 DIABETES MELLITUS, TO ACHIEVE OPTIMAL GLYCAEMIC CONTROL AND PREVENT LONG-TERM COMPLICATIONS

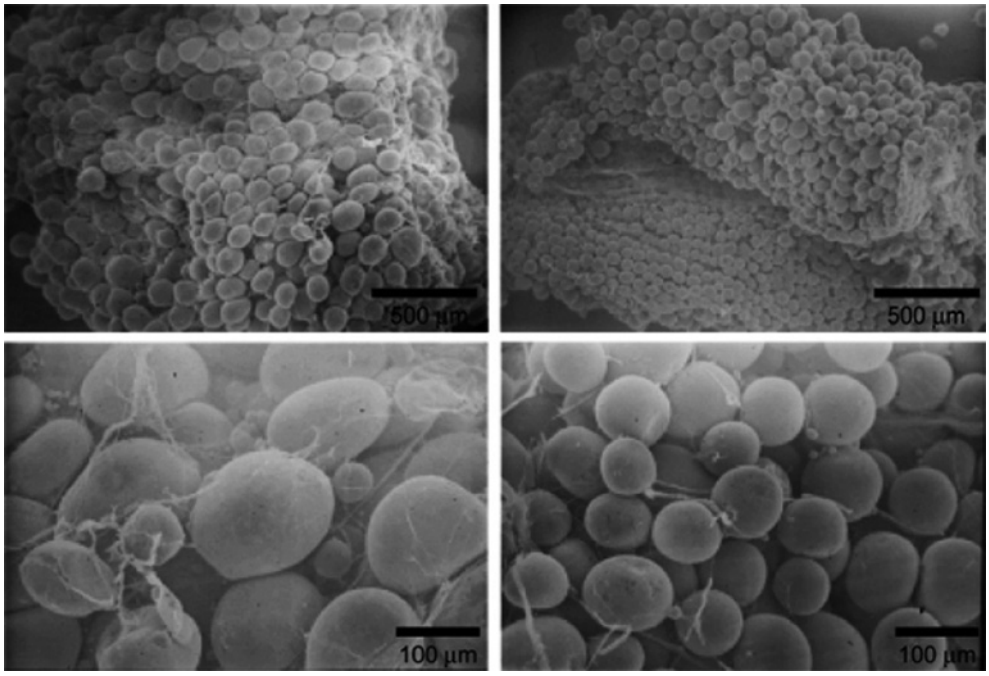


IMAGE 1. HYPERTROPHIC ADIPOCYTES. Scanning electron microscopy of insulin lipohypertrophy (left) and adjacent normal subcutaneous adipose tissue (right) at ×50 (top) and ×100 (bottom) magnification. FITTER Forum 2025.

» red with normal adipose tissue (2). This inconsistent insulin absorption hinders stable glycaemic control and raises the risk of complications.

INSULIN CONSUMPTION

LH is directly associated with higher daily insulin use. PwD with LH often require larger doses to compensate for deficient and unpredictable absorption of insulin (1). The meta-analysis by Mader et al. (2024) found that patients with LH had significantly higher daily insulin consumption (3). Correcting injection technique and resolving LH can lead to substantial reductions in insulin needs (1).

HYPOGLYCAEMIC EPISODES

Erratic insulin absorption from LH-affected areas also increases the risk of hypoglycaemic episodes, especially unexplained ones (1, 3). The above-mentioned meta-analysis showed that patients with LH were significantly more likely to experience unexplained hypoglycaemia (3). These events can be severe and negatively affect quality of life.

DETECTION AND MONITORING OF LH

Detection has traditionally relied on clinical palpation and self-examination, but ultrasound has emerged as a tool with superior performance.

CLINICAL PALPATION AND SELF-EXAMINATION

Clinical palpation by health professionals trained in this skill, together with self-examination by PwD, are first-line methods to detect LH (1). LH is identified as a palpable mass that may be soft or firm (1). However, palpation has significant limitations in accuracy, with a high rate of missed LH compared with ultrasound (2). Although palpation remains accessible and a first-line approach, its lower sensitivity means many LH cases may be overlooked, delaying intervention and prolonging the negative impact on glycaemic control.

ULTRASOUND AS A DIAGNOSTIC TOOL

Ultrasound has proven to be a more accurate diagnostic tool for LH detection than clinical palpation (2). LH shows characteristic ultrasonographic signs, enabling more objective identification. This higher precision is crucial for earlier, more reliable detection, which can lead to timelier interventions and improved glycaemic control (2). Gentile et al.6 identified several LH types by ultrasound features, a classification also described in other studies (7), the most common being:

- **Type A:** with a predominant fibrotic component (***image 2***, courtesy of Amaya ML and Hernández MT). Yellow arrows indicate examples of fibrotic bands (scar tissue) within the disorganised white area that represents the diffuse LH pattern.

- **Type B:** associated with small oedematous islets bordered by fibrous bands (***image 3***, courtesy of Amaya ML and Hernández MT). The image shows a mixed-pattern LH (nodular and fibrotic). The blue area (and other similar darker grey areas) forms the "nodule" or mass of altered fat, and the red areas are the fibrotic "scars" that have formed within that nodule.

Image 4 shows a comparison with an ultrasound without any dermal lesion, courtesy of Amaya ML and Hernández MT.

STRATEGIES FOR PREVENTION AND MANAGEMENT OF LH

Prevention and management focus on patient education and modification of injection technique (1, 2, 4).
Key strategies include:

- **Rotation of injection sites:** Systematic rotation is essential to avoid tissue overload and LH formation (1, 2).

- **No needle reuse:** Needle reuse is a significant LH risk factor. A rando- »

IMAGE 2. TYPE A

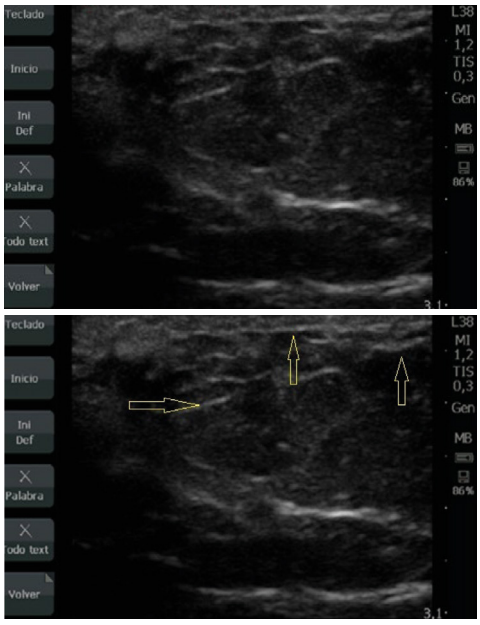


IMAGE 3. TYPE B

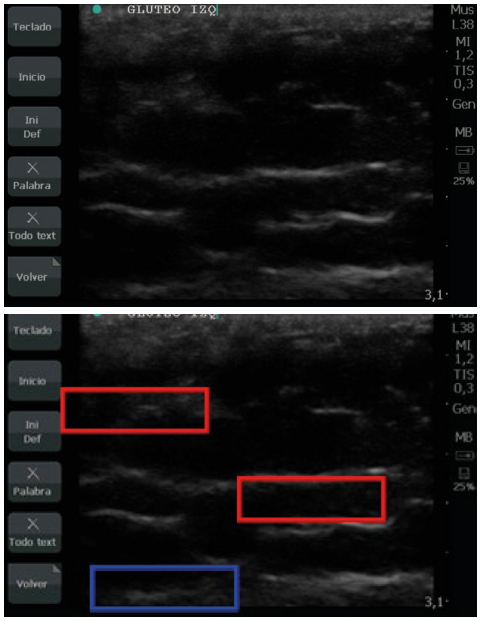
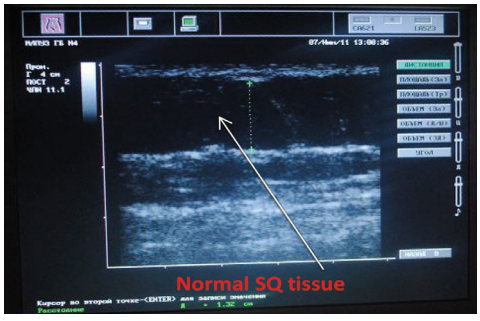


IMAGE 4. NORMAL ULTRASOUND



SYSTEMATIC ROTATION OF INJECTION SITES AND ELIMINATING NEEDLE REUSE ARE ESSENTIAL PRACTICES THAT NOT ONLY PREVENT LH FORMATION BUT CAN ALSO LEAD TO ITS REGRESSION, THEREBY IMPROVING GLYCAEMIC CONTROL AND REDUCING INSULIN NEEDS

» mised clinical trial showed that stopping reuse of syringes and needles significantly reduced LH and improved glycaemic control (4).

- **Use of short needles:** 4-mm needles are safe and effective for most PwD, reducing the risk of tissue trauma (1).
- **Proper injection technique:** Insulin should be injected into healthy subcutaneous fat, avoiding damaged areas (1).

Thus, LH is a prevalent and clinically relevant complication among insulin-using PwD, with a significant impact on glycaemic control. LH contributes to increased glycaemic variability, higher insulin consumption, and more hypoglycaemic episodes. Erratic insulin absorption from LH-affected areas is the underlying mechanism behind these adverse consequences.

LH detection can be substantially improved by using ultrasound, which has proven superior to clinical palpation in diagnostic accuracy. Implementing this tool in clinical practice could facilitate earlier and more precise identification of LH, enabling timely interventions.

Prevention and management strategies are fundamentally educational and focus on optimising insulin injection technique. Systematic rotation of injection sites and eliminating needle reuse are essential practices that not only prevent LH formation but can also lead to its regression, thereby improving glycaemic control and reducing insulin needs. Educational approaches within structured therapeutic education programmes and PwD self-examination are pillars for effective management of this complication.

Moreover, it would be desirable to establish unified protocols to reverse the high prevalence of LH, as countries in our region are beginning to do (8). D

CONCLUSIONS

In conclusion, LH is a critical factor that must be considered in the comprehensive management of diabetes requiring insulin therapy. Greater awareness, more accurate detection, and adherence to best injection practices are imperative to optimise glycaemic outcomes and improve quality of life for PwD.

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