

MATTERS ARISING

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Expanding awareness of potentially life-threatening adverse effects of metformin

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The recent article by Khalaf et al., entitled “Beyond diabetes: harnessing the power of metformin in burn care,” highlights the therapeutic potential of metformin in burn care [1]. In addition to the key points addressed, rare but potentially life-threatening reactions associated with metformin use may warrant further consideration in this clinical context.

Metformin-associated lactic acidosis is a well-recognized but uncommon complication of metformin use, with an estimated incidence of 4.3 cases per 100,000 patients [2]. Additionally, severe hypersensitivity reactions have been reported in association with metformin use. These include anaphylaxis, which is regarded as a rare adverse effect, as well as cases of life threatening angioedema following metformin ingestion. Other allergic reactions have also been reported, including erythema multiforme, bullous pemphigoid, and psoriasiform drug eruption [3–6].

Among the most severe adverse reactions, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

syndrome has been reported, typically presenting with generalized pruritus, rash, lymphadenopathy and eosinophilia [7]. Stevens–Johnson syndrome has likewise been described in association with metformin use [8]. In line with these findings, the National Health Service (NHS) has issued a warning regarding the risk of anaphylactic shock following administration of metformin, a rare event requiring urgent medical attention [9].

Data from the FDA Adverse Reporting System (FAERS) indicate that 8712 cases of skin and subcutaneous tissue disorders potentially associated with metformin use were reported in 2024. The most frequently reported conditions were pruritus ($n=1495$), rash ($n=1209$), hyperhidrosis ($n=1057$), and urticaria ($n=734$) [10]. Similarly, the EudraVigilance database documented 3624 cases of skin and subcutaneous tissue disorders [11].

In conclusion, although life threatening adverse events such as DRESS syndrome, Stevens–Johnson, angioedema and anaphylaxis are rare, they have been reported in association with metformin use [8]. Awareness of these potential complications is essential for clinicians to facilitate early recognition and ensure timely management.

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Competing interests

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References

- Khalaf F, Touma D, Saldanha S, Khalaf G, Barayan D, Jeschke MG. Beyond diabetes: harnessing the power of metformin in burn care. *Crit Care*. 2025;29(1):423. <https://doi.org/10.1186/s13054-025-05662-7>. PMID: 41057939; PMCID: PMC12506066.
- Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with Metformin use in type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2010;2010(4):CD002967.
- Atik D, Büyükcım F, Yılmaz D, Işık B, Demir OF. Angioedema after the first dose of metformin. *Am J Emerg Med*. 2013;31(3):634.e5. <https://doi.org/10.1016/j.ajem.2012.10.021>. Epub 2013 Feb 4. PMID: 23380117.
- Burger DE, Goyal S. Erythema multiforme from metformin. *Ann Pharmacother*. 2004;38:1537. [CrossRef].
- Pokharel N. Metformin induced bullous pemphigoid—A rare case report. *J Pak Assoc Dermatol*. 2022;31:740–3.
- Koca R, Altinyazar HC, Yenidünya S, Tekin NS. Psoriasiform drug eruption associated with metformin hydrochloride: A case report. *Dermatol. Online J*. 2003;9:11. [CrossRef].
- Voore P, Odigwe C, Mirrakhimov AE, Rifai D, Iroegbu. N.A. DRESS syndrome following metformin administration: A case report and review of the literature. *Am J Ther*. 2016;23:e1970–3. [CrossRef] [PubMed].
- Kowalska J, Wrześniok D. Skin-Related Adverse Reactions Induced by Oral Antidiabetic Drugs-A Review of Literature and Case Reports. *Pharmaceuticals (Basel)*. 2024;17(7):847. <https://doi.org/10.3390/ph17070847>. PMID: 39065698; PMCID: PMC11280276.
- Health Service Executive (HSE). Side effects of metformin. Supplied by the NHS and adapted for Ireland by the HSE. Dublin: HSE. 2024 Jun 9. Available from: <https://www2.hse.ie>
- FDA AdverseEvents Reporting System (FAERS) Public Dashboard. Available online: <https://fis.fda.gov/sense/app/95239e26e0be-42d9-a960-9a5f7f1c25ee/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis> (accessed on 7 May 2024).
- EudraVigilance—European Database of Suspected Adverse Drug Reaction Reports. Available online: <https://www.adrreports.eu/en/search.html> (accessed on 7 May 2024).

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