LETTER TO THE EDITOR

# Reply to Musarrat et al

*Ming-Ching Shen**

Sir,

It is well documented that metformin use may cause vitamin B12 deficiency,[1,2] which may lead to hyperhomocysteinemia,[3] particularly when folate deficiency, B12 deficiency or methylenetetrahydrofolate reductase (*MTHFR*) homozygous C677T mutation is also present, based on the metabolic pathway of homocysteine.[3] It was estimated that 5.6–7.3% of diabetic patients taking metformin might develop evidence of B12 deficiency.[1] Higher metformin dose and longer treatment duration as well as increased age and vegetarianism were shown to be independent risk factors of vitamin B12 deficiency.[2] Other confounding factors include uncontrollable supplement of vitamins or trace elements in food or any daily elements.[4] The prevalence of *MTHFR* C677T homozygous mutation was reported to be 5–12% in a White population and 6–8% in Taiwanese Chinese,[5] and the homozygous mutation is related to hyperhomocysteinemia when lower plasma folate level coexists, but not when plasma folate level is higher.[6] Hence, it has been reported that homocysteine level may[3] or may not[4] increase during metformin treatment; many confounding factors result in such conflicting data. Findings in the one case report[7] meant to call attention to the clinical evidence that hyperhomocysteinemia caused by a metformin-induced vitamin B12 deficiency and a *MTHFR* C677T homozygous mutation may serve as an additional independent risk factor for vascular thrombosis in diabetic patients, although many patients are on metformin therapy without significant problems.

## References

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