Reply

Dear Editor,

We thank the readers for showing interest and commenting on our article.

From the last paragraph of the letter it seems that the impression gained from the article is that we advocate the use of the hand held lactate meter as a replacement of the arterial blood gas (ABG) machine. This is incorrect as we have compared the results obtained from both the machines in an effort to validate the results obtained from the hand held machine.

Providing an ABG machine in all field settings may not be economically feasible, moreover, even provision of the basic support systems for the ABG machines (which do require extensive service and engineering back up) may not be possible everywhere. It is in these settings where the hand held lactate meter would provide invaluable inputs for resuscitation and follow up of patients suffering from the sepsis syndrome. We therefore in fact do not consider it as a

limitation of the study. Moreover, we would also not agree that 'field settings are resource limited'. Compared to any other health care organization in the country, AFMS field hospitals are very well equipped with pulse oximeters, transport ventilators, infusion pumps, etc. provided from various sources. Therefore, provisioning of handheld lactate meters at the periphery is very much possible and economical.

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Letter to the Editor

Metabolic syndrome and BPH: What do we know?

Dear Editor,

At the outset, I offer my compliments to the authors of the original article "Association between components of metabolic syndrome and prostatic enlargement: An Indian perspective" by Nandy et al. in *Med J Armed Forces India* 2016;72:350–355.¹ The authors in this present article have delved into an unexplored subject as far as the Indian subcontinent is considered and have thus added to the Indian database, which is lacking on the subject. They have brought to light the association of metabolic syndrome with that of the prostatic volume and Lower Urinary Tract Symptoms (LUTS), in the Indians, an ethnically different subpopulation. Although the subject of the article has been taken well, the presentation, however, lacks the lustre to attract the readers and has also failed to discuss the plausible mechanisms whereby the metabolic syndrome leads to the development of Benign Prostatic Hyperplasia (BPH). This not only leaves the readers wanting for more but also makes the article to look incomplete.

There have been a number of publications which have established the association of BPH with that of metabolic syndrome. But the exact mechanism which leads to the development of BPH in this subset of patients with metabolic syndrome is not clear. Various researchers have proposed different theories which include, but are not restricted to, changes in insulin resistance, increased autonomic activity, impaired nitrergic innervation, increased Rho kinase activity,

pro-inflammatory status and changes in sex hormones that occur in association with metabolic syndrome. However, the exact underlying mechanisms that regulate the potential relationship between MetS and BPH/LUTS still need to be clarified. Recently, Vignozzi et al. introduced an interesting three-hit hypothesis on the development of BPH in such subgroup of patients.² This hypothesis proposes that an overt or sub-clinical inflammation which is the first hit could be overlapped by the metabolic alternations in the body – the second hit and changes in sex-hormone levels and the third hit, leading to the over-expression of toll-like receptors, transformation of prostatic cells into antigen-presenting cells and up-regulation of growth factors (andromedins), resulting in prostate enlargement.

Hyperinsulinaemia, which is one of the most common derangements found in metabolic syndrome, leads to increased sympathetic activity, which in turn leads to smooth muscle contraction throughout the genitourinary tract contributing to the LUTS.³ Hyperinsulinaemia may also indirectly increase the risk of BPH by increasing the level of insulin-like growth hormone 1.³

The elevation of pro-inflammatory markers in metabolic syndrome tends to reduce the synthesis of nitric oxide (NO) in the endothelial cells. The reduced NO activity in the prostate in turn leads to smooth muscle proliferation, prostatic enlargement and thus contributes to LUTS.³

The association of altered lipid profile, especially high serum triglycerides and low serum High Density Lipoproteins

(HDL) cholesterol with increased prostate volume has been reported earlier. The proposed pathway of causation is induction or maintenance of an inflammatory state within the prostate leading to triggering of cell growth. The authors have reported a similar finding in their study, where high serum triglyceride and low serum HDL levels were significantly associated with increased prostate volume (Table 2). However, during the discussion, they have taken a contrarian view and said that they did not find any correlation between BPH and serum HDL levels. This association was first established in rats in the year 2007 by Rahman et al. where they reported a significantly higher prostatic weight in hyperlipidemic rats (2.6 vs 1.4 g; $p < 0.01$).⁴ Subsequently, this fact has been strengthened in human studies also. Hammarsten et al. reported a mean prostate volume of 49 ml vs 39 ml in patients with low serum HDL levels as compared to those with normal serum levels. They also reported a higher annual BPH growth rate in such individuals.⁵ Hence, I would like to know, whether this was an unintentional error or the authors want to bring out the fact that these two factors were not associated.

The Rho kinase system plays an important role in the maintenance of tonic contraction and may contribute to prostate contractility. Many of the components found in patients of metabolic syndrome, such as autonomic hyperactivity, impaired NO activity, elevated IL-8 level and elevated endothelin-1 levels, may favour the activity of the Rho kinase system. This in turn results in a higher prostate contractility and LUTS.³

Hence, knowing about the plausible mechanisms for causation of BPH in patients with metabolic syndrome is important, as it may provide newer insights in developing new treatment and prevention protocols, as rightly pointed out by the authors in their concluding sentences.

Reply

Dear Editor,

The authors wish to place on record their appreciation of the interest shown on their article by the discerning reader. We thank the respondent for his/her insightful comments.

The main purpose of the present study was to find relationship between prostate gland volume and various components of metabolic syndrome in Indian population and thereby perform a BPH risk factor analysis.

Besides ageing and androgen, inflammation is linked to the development of BPH. Metabolic syndrome, which promotes systemic inflammation and oxidative stress, mediates the connection. It is possible that BPH represents a non malignant proliferative pathway promoted by oxidative stress and inflammatory mediators. However the exact underlying mechanism that regulates the potential relationship between Met S and BPH/LUTS still need to be clarified as rightly brought out by the reader.

The high serum TG and low serum HDL were significantly associated with increased prostate volume and our apology for

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the unintentional error. We thank the respondents of the letter for their valuable comments.

FURTHER READING

1. Abdollah F, Briganti A, Suardi N, et al. Metabolic syndrome and benign prostatic hyperplasia: evidence of a potential relationship, hypothesized etiology and prevention. *Korean J Urol*. 2011;52(8):507–516.

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