

Correspondence

What's in a name—25(OH)D or 25(OH)D₃?

In the report by Tandon *et al.*¹ documenting the bone mineral parameters in healthy young Indian adults, the authors focus on the 25-hydroxyvitamin D [25(OH)D] status of the study group and the interrelationships between biochemical and bone mineral density (BMD). In fact, there are no assays available to detect 25-hydroxyvitamin D₃ exclusively. The commercially available kit (DiaSorin, Incstar Corporation, Stillwater, MN, USA) used by the authors quantifies 25-hydroxyvitamin D, i.e. 25-hydroxy ergocalciferol {vitamin D₂ [25(OH)D₂] and 25-hydroxy cholecalciferol {vitamin D₃ [25(OH)D₃]}. In this method, the primary antibody which is added reacts equally with 25(OH)D₂ and 25(OH)D₃.² Hence, the terminology '25(OH)D' is preferred. In effect, the authors have estimated '25-hydroxyvitamin D' and not '25-hydroxyvitamin D₃' as mentioned in the article.¹

One should also be cautious about the fact that 'population-based reference values' (e.g. derived from blood donors, etc.), developed by the kit manufacturers are depicted as a 'reference range' and are usually employed to define vitamin D deficiency. These values are limited by climate, exposure to sunshine, clothing habits, among others, and could therefore vary according to other local conditions. Another problem is that different investigators use different 'reference populations'. These 'population-based reference values' provided by kit manufacturers may lead to fallacious interpretation of the values in different regions of the world. A 'functional health-based reference value' based on the levels of vitamin D and parathyroid hormone (PTH) has been proposed by Lips.³ This defines vitamin D deficiency as 'the critical level of 25(OH)D which prevents secondary hyperparathyroidism'. Staging of vitamin D deficiency is based on 25(OH)D levels, increase in serum PTH and changes in bone histology. Mild vitamin D deficiency is defined as 25(OH)D levels of 10–20 ng/ml, 15% increase in the PTH level, and normal or high turnover in bone histology. Moderate vitamin D deficiency is defined as 25(OH)D levels of 5–10 ng/ml, 15%–30% increase in the PTH level, and high turnover in bone histology; severe vitamin D deficiency as 25(OH)D levels <5 ng/ml, >30% increase in the PTH level, and mineralization defect/incipient or overt osteomalacia in bone histology. These are based on seasonal variations of PTH, which are no longer visible at the corresponding 25(OH)D levels.^{4,5} This is again based on vitamin D supplementation studies done by various groups and correlation with bone histomorphometric studies.⁶ This classification encompasses the 'vitamin D–calcium–PTH axis' and its impact on bone. It is more apt and based on scientific reasoning.

The authors have used 'population-based reference values'. The reference range given by the manufacture is on a group of 44 midwestern Caucasian volunteers in the age group of 23–67 years.⁷ On application of a 'functional health-based reference value' it can be seen that some of them might come under the category of mild vitamin D deficiency. This might well explain the raised serum alkaline phosphatase and PTH levels in some of them.

Another point of interest is the BMD data. The accompanying editorial⁸ states that dual-energy X-ray absorptiometry (DEXA) is the 'gold standard' for the diagnosis of osteoporosis. In the editorial,⁸ it has also been argued that Indian norms for BMD have to be developed. However, methodologically, DEXA has its limitations. The software used with the equipment is calibrated for the western population and the same used to measure the BMD of the Indian population. It amounts to propagation of 'systematic error'. These

points should be considered while interpreting the data and also while developing Indian norms. In the Indian context, a low BMD might convey that the bones are osteopenic or osteoporotic, but a normal BMD does not mean that the bones are normal. This is especially true in India where 13 states have been declared endemic for skeletal fluorosis.⁹ Bone histomorphometry studies of bone biopsies in patients with endemic skeletal fluorosis do not correlate with skeletal X-rays, leave alone BMD.

In the patients studied by Tandon *et al.*, osteopenia by BMD could probably be related to vitamin D levels if the 'functional health-based reference value' is used. Osteoporosis in young healthy subjects in their third decade of life warrants further investigations to look for rarer causes. It is well known that haematological disorders can present with severe osteoporosis. An in-depth study of the bone marrow in these patients would be more helpful. Analysing such patients separately from the osteoporotic group may give more information.

Looking back at the data in the background of the 'functional health-based reference value' of vitamin D, this paper has documented mild vitamin D deficiency at least in some young, healthy Indian men and women.

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Authors' response

We would like to thank Dr Harinarayan for his constructive comments. We agree with him that the vitamin D kit used by us (DiaSorin) indeed measures both 25-hydroxyvitamin D₃ and -D₂. 25-hydroxyvitamin D₃ is the predominant form of 25-hydroxyvitamin D in the blood. Hence, conventionally and by precedence, the term

used has been 25-hydroxyvitamin D₃. Dr Harinarayan has also used the term 25-(OH)D₃ while referring to the analyte measured by a similar kit based on radioimmunoassay.¹

Once again, we agree with the comment that two concepts, namely 'population-based reference range' and 'functional health-based reference value' are used when discussing vitamin D deficiency. While there is no doubt that the population-based reference range will be influenced by several extraneous factors and so cannot necessarily be extrapolated to different regions of the world, this range has been used in earlier publications when discussing hypovitaminosis D. There also appear to be differences in opinion as to what constitutes 'functional vitamin D deficiency'. In the review by Lips,² different studies refer to different possible cut-offs in the range 10–30 ng/ml for defining a functionally low vitamin D level. Also, most of the analyses to arrive at a reference value of vitamin D deficiency comes from studies conducted in the elderly who do not have the same responses to the vitamin D–parathyroid hormone (PTH) axis as healthy young adults. Since this issue is far from resolved, the population-based reference range is equally acceptable for defining vitamin D deficiency as is the case for several other analytes. With specific reference to the 9 subjects with elevated alkaline phosphatase, the break-up of their vitamin D levels shows (as per Lips classification): 4 to have mild vitamin D deficiency and 5 to have normal vitamin D levels; none had levels below the normal range of the kit. This does not support the speculation of Harinarayan. Hence, we also do not agree with his last statement that the paper brings out mild vitamin D deficiency in some healthy young Indian adults. Further, Harinarayan makes an erroneous observation, namely, that there were cases with elevated PTH levels. We clearly state that there was no subject with an elevated PTH level (p. 299, right column, para 2, line 1).³

With regard to bone mineral density (BMD), we agree with Harinarayan's statement about the possible limitation of dual-energy X-ray absorptiometry (DEXA) in a country with endemic fluorosis. We have also raised the issue in our article for the need to establish ethnically appropriate BMD norms. We, however, do not agree with his speculation of the possibility haematological disorders, since the study was conducted in a group of healthy paramilitary personnel who undergo regular (at least annual), thorough, physical examination.

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II

I appreciate Dr Harinarayan's interest in the report by Tandon *et al.*¹ as well as in the accompanying editorial.² In response to Dr Harinarayan's comments, I would like to make the following points:

1. It is true that the DiaSorin assay for serum 25(OH)D (or D₃!) measures the levels of both 25-hydroxyvitamin D₂ and 25-hydroxyvitamin D₃. However, the radioimmunoassay measurements predominantly reflect the levels of D₃, which contributes 93%–94% to the assessment of nutritional vitamin D status. It is, therefore, common practice to use the terms interchangeably. The 2003 edition of the American Society for Bone and Mineral Research *Primer*^{3,4} continues to refer to the analyte measured as 25(OH)D₃.
2. I agree with Dr Harinarayan when he refers to the Lips' classification. The reference ranges used by manufacturers do not truly reflect 'normal' values. This does not, however, take away from the conclusions of Tandon *et al.* As compared to published data on serum 25(OH)D levels in Indians, overall, Dr Tandon's group clearly had far better data on the nutritional vitamin D status of Indians. The essential message that Indians can synthesize adequate amounts of vitamin D if exposed to enough sunlight is important and should not be lost in the debate over what constitutes normal.
3. It is true that no technique for estimating bone mineral density (BMD) is foolproof. However, at present, dual-energy X-ray absorptiometry (DEXA) continues to be the best and most widely used method. In fact, the WHO classification⁵ of osteoporosis incorporating T scores is based on the DEXA technique. Fluorosis can certainly interfere with BMD estimations, but this applies to all available techniques and is not specific for DEXA. It would be appropriate for studies from India to ideally measure the urinary fluoride levels also, at least in subjects who hail from areas known for fluorosis.

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Body mass index, waist circumference and waist–hip ratio: Findings from an urban community survey, Tamil Nadu

We read with interest the article by Kurpad *et al.* who evaluated the correlation between waist circumference and waist–hip ratio to body mass index (BMI).¹ However, since this was a hospital-based study and the number of obese subjects was small, the results need to be confirmed in a larger population. In this context, we attempted to verify the relationship between BMI, waist circumference, waist–hip ratio and hip circumference among women >20 years of age using the urban data from our study on obesity among women in southern India by the Coimbatore Diabetes Foundation in 2003.

Our study was a community survey designed to quantify the problem of obesity, its relationship to eating pattern, physical activity, demographic pattern, reproductive health history, community perception of obesity and community awareness of complications of obesity among women >20 years of age. The urban sample was selected in two stages. Primary sampling units were wards selected randomly from the list of the intensive coverage area of the Urban Health Centre of P.S.G. Hospitals, Coimbatore, Tamil Nadu, followed in the second stage by selection of households using simple random sampling within each selected primary sampling unit. A total of 537 women were interviewed and examined.

The relationship between anthropometric measurements was analysed by calculating the Pearson product moment correlation coefficients using SPSS for Windows, version 10.1. Of the 311 overweight women (BMI >23 kg/m²), 241 (66.4%) had abdominal obesity according to the waist-hip ratio (lower cut-off >0.8) while 252 (86.3%) had obesity by the waist circumference criterion (lower cut-off >80 cm). The correlation between waist circumference and BMI was 0.731 (p<0.01), between hip circumference and BMI 0.704 (p<0.01) and waist-hip ratio and BMI 0.266 (p<0.01).

These results clearly indicate that waist circumference correlates better with BMI than waist-hip ratio and support the findings of Kurpad *et al.*

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Scientific writing skills of medical personnel in India: An evaluation

Introduction

Scientific communication, written and oral, is an essential skill for all scientists. However, no formal training in this field is imparted in our medical schools. It is probably assumed that the students will pick up these skills by themselves as they undergo training in various components of the medical curricula. However, the efficacy of this approach is not known. Little information is available on the knowledge about scientific writing and communication among medical personnel in India. We, therefore, decided to evaluate the knowledge about scientific writing and communication skills of medical personnel.

Methods

Participants attending a 2-day workshop on scientific communication were requested to complete a questionnaire at the beginning of the workshop.

Results

All the 32 workshop participants responded to the questionnaire and represented a wide cross-section of age, research and publication experience, and medical specialties. Two respondents did not provide demographic details; the remaining 30 participants were 23-43 (median 31) years of age and included 8 serving or retired faculty members from various institutions, 7 senior residents, 4 junior residents, 3 scientists, 3 senior research fellows, 1 senior medical officer, 3 PhD students and 1 editorial staff member of a medical journal. Most (24 of 30) participants had published one or more scientific papers (median 4; range 0-100).

Of a maximum possible score of 100 for the 10 questions asked, the median score was 62 (range 16-78). Nine of the 32 (28%) participants had a score below 50. Responses to some of the individual questions are shown in Table I. The total scores obtained by the respondents had no significant correlation with their age ($r = -0.32$; $p = \text{ns}$).

TABLE I. Responses to individual questions in the survey

Question	Response	n
Name 3 indexing services	Two correct responses	12
	One correct response	15
	No response	5
Name 3 indexed Indian medical journals	Three correct responses	18
	Two correct responses	4
	One correct response	7
	No correct response	3
List components to be included in the cover page	Correct	4
	Incorrect	28
List components of a structured abstract	Complete correct response	3
	Incomplete but correct	21
	None	8
Name the source of keyword terms	'Medical Subject Headings'	6
	Index Medicus	8
	None	18
Name 4 parts of a scientific paper	All four correctly named	30
	Not correctly named	2
Provide abbreviations for 8 units of measurement	All correct	3
Provide abbreviations for names of 7 medical journals	All correct	0
	5-6 correct responses	4
	3-4 correct responses	9
	1-2 correct responses	14
	None	5
Proofreading marks for 7 types of corrections	All correct	2
	5-6 correct responses	5
	3-4 correct responses	8
	1-2 correct responses	6
	None	11
Indicate whether the following statements are true or false:		
1. References may be used in the abstract	correct responses	29
	incorrect responses	3
2. All the important words in the title should be mentioned as keywords	correct responses	15
	incorrect responses	17
3. References are cited in alphabetical order	correct responses	22
	incorrect responses	10
4. Tables should be typed in the manuscript where they are to appear in the text	correct responses	23
	incorrect responses	9

Discussion

Our data show that medical and biomedical researchers in India have very limited knowledge of various aspects of scientific writing, including uniform requirements for submission of manuscripts, and of the usual conventions followed. This is particularly disturbing

since most of the respondents had published one or more papers in the past and were engaged in research. We were unable to find any published data on the subject.

This lack of writing skills may inhibit our scientists from reporting their research findings. Also, it may reduce the chances of acceptance of their manuscripts. We therefore believe that there is a need to include formal teaching of scientific writing in medical and research training. In fact, our institution runs such a course for its students annually, though attendance at the course is optional.

In the absence of published data, we were unable to compare Indian biomedical scientists with those in other parts of the world. It may be interesting to study this aspect in other geographical regions and to conduct a similar survey in the future to look at time trends in the awareness of writing skills.

Though our data may not be generalizable, since the workshop participants may have preferentially included those who lacked writing skills and hence decided to attend the workshop, they provide useful information.

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In vitro activity of vancomycin and teicoplanin against staphylococci in intensive care units

Infections caused by antibiotic-resistant Gram-positive bacteria, especially methicillin-resistant staphylococci, have increased during the past two decades in most areas of the world. Severe nosocomial infections caused by these organisms are treated with either vancomycin or teicoplanin.^{1,2} We evaluated the antimicrobial activity of vancomycin and teicoplanin against methicillin-resistant staphylococci isolated from patients in 3 surgical intensive care units (SICUs) over 4 months in Istanbul. One of the SICUs specialized in cardiovascular surgery and the other two had different fields of surgical activity.

One hundred and twenty nosocomial methicillin-resistant strains of staphylococci were isolated from clinically important materials, e.g. blood (two or more blood cultures), central venous catheter, wound and normally sterile body fluids, in the presence of clinical manifestations not attributable to other causes after at least 72 hours of hospitalization. The Bactec 9050 Blood Culture Instrument (Becton Dickinson, Baltimore, USA) was used for analysing blood cultures. There were 63 (52.5%) *Staphylococcus aureus* and 57 (47.5%) coagulase-negative staphylococci (CNS). All isolates were identified by conventional methods³ and confirmed by the

API 32 Staph system (BioMérieux, France). Methicillin resistance was confirmed using the oxacillin E-test (AB Biodisk, Solna, Sweden) on a medium containing 2% NaCl. After identification, all isolates were maintained in tryptic soy broth containing 10% glycerol at -70 °C until further testing. Susceptibility testing of each isolate for vancomycin and teicoplanin was performed using the E-test (AB Biodisk, Solna, Sweden) according to the National Committee for Clinical Laboratory Standards (NCCLS) guidelines.⁴ *Staphylococcus aureus* ATCC 29213 was used as the control strain.

The majority of microorganisms were isolated from the blood ($n=56$; 46.7%) and central venous catheters ($n=29$; 24.2%). The others were cultured from wounds, abscesses ($n=13$; 10.8%), drainage fluids ($n=12$; 10%) and other materials ($n=10$; 8.4%). There were 5 species of CNS among the isolates: *Staphylococcus epidermidis* (42), *Staphylococcus hominis* (6), *Staphylococcus haemolyticus* (6), *Staphylococcus intermedius* (2) and *Staphylococcus xylosum* (1). All the isolates were nosocomially acquired.

None of the 120 Staphylococcal isolates were resistant to vancomycin but 6 samples of *S. haemolyticus* were resistant to teicoplanin. The minimum inhibitory concentration (MIC₅₀ and MIC₉₀) values for *S. aureus* and CNS isolates were 2 µg/ml, 2 µg/ml, 2 µg/ml and 2 µg/ml for vancomycin, and 3 µg/ml, 8 µg/ml, 4 µg/ml and 8 µg/ml for teicoplanin, respectively. All the *S. haemolyticus* had MICs of 256 µg/ml for teicoplanin and 4 µg/ml for vancomycin.

In recent years, decreased susceptibility of *S. aureus* and CNS isolates to glycopeptides has been reported. Of the CNS species, *S. epidermidis* and *S. haemolyticus* are affected by the development of resistance. Although the majority of CNS remain susceptible to vancomycin, isolates with reduced susceptibility have been observed. Reduced susceptibility to teicoplanin is observed in about 30% of *S. haemolyticus* and less often in *S. epidermidis*.⁵

Vancomycin-intermediate or -resistant *S. aureus* isolates are not found in Turkey. Rarely, teicoplanin-intermediate or -resistant CNS have been detected in Turkey.^{6,7}

Vancomycin is a good choice for the treatment of severe infections caused by CNS in SICU patients. There is a need for surveillance of nosocomial CNS developing resistance to glycopeptides.

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