

# First Reported Cases of Exercise-Associated Hyponatremia in Asia

## Authors

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## Key words

- hydration
- marathon
- ultra-marathon

## Abstract

There are no reported cases of exercise-associated hyponatremia (EAH) in tropical Asia. This study aimed to investigate the incidence of EAH at the on-site medical tent and fluid balance in long distance foot races in a warm and humid environment. Body mass was taken before and after the races (42-km marathon; 84-km ultra-marathon). Blood sodium concentration was measured for symptomatic runners admitted to the medical tent. Mean (SD) dry bulb temperature was 29.0 (0.6)°C, relative humidity 89 (2)% and wind speed 0.3 (0.5) m/s. Three out of the 8 symptomatic run-

ners admitted to the medical tent were diagnosed with hyponatremia, with blood sodium concentrations of 134 mmol/L in a 42-km runner, and 131 and 117 mmol/L in two 84-km runners. In the 42-km race, mean %  $\Delta$ BM was -1.6 (1.2)%, ranging from -5.7 to 1.4%, and 22 runners (7%) gained weight. In the 84-km race, mean %  $\Delta$ BM was -2.3 (1.7)%, ranging from -8.0 to 1.4%, and 9 runners (8%) gained weight. In addition to the 3 cases of symptomatic hyponatremia observed, 8% of the 84-km runners and 7% of the 42-km runners gained weight during the race. This indicates the need to disseminate advice for the prevention and treatment of EAH for races held in the tropics.

## Introduction

Exercise-associated hyponatremia (EAH) is defined by a serum or plasma sodium concentration below 135 mmol/L [19] during or up to 24 h after prolonged physical activity [1,3]. This condition may manifest symptomatically [3] or asymptotically [18]. Although the severity of neurological signs and symptoms generally increases with lower sodium concentrations [2], great individual variability renders the numerical value of sodium concentration an unreliable predictive index of the clinical severity of EAH [12,39]. The early symptoms of EAH include bloating, puffiness, headache, nausea and vomiting [3,15,22,34]. Many of these are non-specific and can occur following prolonged exercise in the absence of EAH, prompting the need to measure blood sodium concentration for accurate medical diagnosis. Severe symptoms present during exercise-associated hyponatremic encephalopathy, and include alteration of mental status (e.g. confusion, disorientation, agitation, and delirium), seizures, respiratory distress, obtundation, coma and death [13]. The prevention and treatment of EAH is led by international experts

from the scientific community, with the formulation of the 1<sup>st</sup> International EAH Consensus Development Conference Statement in 2005 [11], and an updated consensus statement in 2008 [13].

Exercise associated hyponatremia was first reported in a 46-year-old female and a 37-year-old male in the 1981 88-km Comrades Marathon [26]. Exercise-associated hyponatremia has subsequently been recognised as an important cause of race-related death and life-threatening illness [1]. Fatalities have been reported in the 1993 Valley of the Giants Marathon, 1998 Chicago Marathon, 2002 Boston Marathon, 2002 Marine Corps Marathon and 2007 London Marathon [15,23,28,31]. Prolonged exercise spanning more than 4 h has since been recognised as a risk factor for EAH [1,3,13,34]. Reports of EAH in marathons and ultra-endurance events have been documented in Africa [14,26,32,33], Europe [9,18], North America [1,8,15,20,31] and Oceania [34,35,36], but not in Asia. In addition, few of these studies occurred in warm and humid environments [8,9,20] despite the recognition of unusually hot environmental conditions as a risk factor for EAH [13].

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## Bibliography

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Body mass changes during exercise provide an estimation of athletes' hydration status, and their awareness and adherence to current position stands on hydration during exercise [5, 30]. The primary cause of EAH is the consumption of fluid in excess of urinary and sweat losses, which is discernible with a gain in weight [1, 34]. Athletes should expect to lose weight during exercise and never to gain weight [24].

Singapore is located at 1° north of the equator and its climate is classified as "equatorial", with no distinct season throughout the year. The weather is warm and humid, with daily temperature ranging between 26°C and 32°C. Peak temperature is achieved at about 1300h daily. The lowest relative humidity of ~60% is usually achieved during peak ambient temperature at the noon hour, and peak relative humidity reaches >85% between 0100h and 0200h daily. The Adidas Sundown Marathon in Singapore is an annual overnight foot race that comprises the full- (42 km) and double-marathon (84 km) categories. This study aimed to evaluate the prevalence of EAH in athletes admitted to the on-site medical tent following participation in an overnight marathon or an ultra-marathon in a warm and humid climate, and to profile their hydration status by quantifying changes in body mass resulting from the race. To our knowledge, this is the first investigation of EAH in Asia.

## Materials and Methods

### Study population

Ethical approval was granted by the ethical review board of the Singapore Sports Council and conformed to the international standards required by the journal [10]. Volunteers competing in the 42-km and 84-km races gave their verbal consent to participate in this study on-site at the start and end of their race.

### Study setting

The Adidas Sundown Marathon 2009 was held in eastern Singapore, on a relatively flat course along a seaside park and the city road. Race categories investigated were the 42-km marathon and 84-km ultra-marathon. Twenty fluid stations were positioned along the 42-km route, and provided sports drink (248 kcal/L, carbohydrate 62 g/L, sodium 20.9 mmol/L, potassium 3.4 mmol/L) and water (Ice Mountain Mineral Water, Fraser and Neave, Limited). The 84-km race route comprised of 2 loops of the 42-km course, corresponding to 40 fluid intake opportunities for the ultra-marathon runners. The ultra-marathon race commenced at 1900h on May 30, 2009, and the marathon race commenced 5 h later, at midnight.

## Measurements

Pre-race body mass was recorded within the hour before race start. Post-race body mass was obtained immediately after completing the race (<1 min), and within 10 m of the finish line to avoid fluid consumption prior to its measurement. Body mass was measured in racing attire using a digital platform balance (Seca, Hamburg, Germany) with an accuracy of 0.1 kg. The percent body mass change (%  $\Delta$ BM) for each runner was calculated by [(post-race body mass – pre-race body mass) / pre-race body mass] x 100. Blood samples (2 mL) were collected from symptomatic runners admitted to the on-site medical tent and analysed in duplicate for sodium, potassium, chloride and blood urea nitrogen (BUN) concentrations using a hand-held i-STAT blood analyser (i-STAT 6+ cartridge, 06F05-01; i-STAT System, Abbott Point of Care, NJ). The reliability of the hand-held i-STAT blood analyser has been established by comparison with a standard laboratory electrolyte analyser [7].

## Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 15.0 for windows was used for statistical analysis. Paired t-test was used to analyse differences between pre- and post-race body mass and independent t-test was performed on participants' %  $\Delta$ BM between the 42-km and 84-km races. Relationship between finishing time and %  $\Delta$ BM was analysed using Pearson's product moment correlation coefficient (*r*). Data in this study are presented as mean (SD). Statistical significance was accepted when *P*<0.05.

## Results

The average dry bulb temperature during the race was 29.0 (range: 28.3–30.2)°C, with relative humidity 89 (86–93) % and wind speed 0.3 (0–1.5) m/s. Six-hundred and two runners started the 84-km race and 407 (68%) runners finished successfully, while 5593 runners started the 42-km race and 4659 (83%) runners completed. From the 6195 runners in both races, both pre-race and post-race body mass data for 417 participants (106 in 84-km men, 8 in 84-km women, 265 in 42-km men and 38 in 42-km women) were obtained.

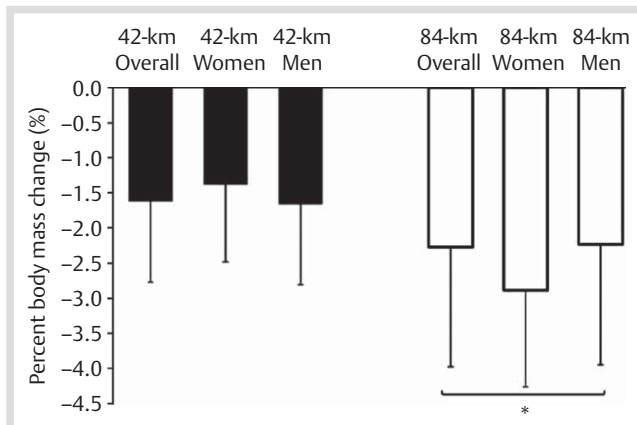
## Exercise-associated hyponatremia

Eight symptomatic runners were admitted to the medical tent and were attended to by medical doctors on-site. Three participants had blood sodium concentrations below 135 mmol/L and were diagnosed with EAH (● Table 1). The symptoms observed were bloating, puffiness, confusion, nausea and vomiting. Only

**Table 1** Blood analyses of the 8 runners who were admitted to the medical tent. 3 runners displayed blood sodium concentrations below 135 mmol/L and were diagnosed with symptomatic EAH.

Patient No.	Category	Sex	Finishing time (h:min:s)	Na <sup>+</sup> (mmol/L)	K <sup>+</sup> (mmol/L)	Cl <sup>-</sup> (mmol/L)	BUN (mg/dL)
1	42-km	male	4:03:18	134	4.1	104	21
2	84-km	male	8:02:00	131	4.3	101	24
3	84-km	male	11:16:31	117	5.6	90	20
4	84-km	male	11:52:45	138	3.6	101	16
5	84-km	male	12:04:57	140	3.9	106	22
6	84-km	male	12:11:18	143	3.8	108	18
7	84-km	female	DNF*	139	3.8	107	20
8	84-km	male	DNF <sup>†</sup>	143	4.0	107	15

DNF: Did not finish. \* Stopped at 50 km. <sup>†</sup> Stopped at 55 km



**Fig. 1** Percent body mass change. Mean values ( $-SD$ ) are shown. All displayed significant decrease in body mass from the race ( $P < 0.001$ ). \* A greater decrement in mean %  $\Delta$ BM was observed after the 84-km race than the 42-km race ( $P < 0.01$ ).

Patient 2 had his pre- and post-race body mass recorded. He gained 0.9 kg (1.2% increase in body mass) over the 84-km race, while the mean  $\Delta$ BM for his race category was  $-1.4$  (1.1) kg. He finished 5<sup>th</sup> in the 84-km race.

### Body mass change

All categories displayed significant decreases in body mass (● **Fig. 1**;  $P < 0.001$ ). Mean pre-race body mass for those profiled in the 42-km category was 66.0 (9.3) kg, and mean post-race body mass was 64.9 (9.2) kg. Mean pre-race body mass for the volunteers profiled in the 84-km category was 64.4 (8.9) kg, and mean post-race body mass was 63.0 (9.0) kg. A greater decrement in mean %  $\Delta$ BM was observed after the 84-km race than the 42-km race ( $P < 0.01$ ).

In the 42-km race, %  $\Delta$ BM ranged from  $-5.7$  to  $1.4\%$  and 53% of the runners profiled displayed between  $-2$  to  $0\%$   $\Delta$ BM (● **Table 2**). Eight percent (21 out of 265) of the men and 3% (1 out of 38) of the women had %  $\Delta$ BM  $> 0$ . In the 84-km race, %  $\Delta$ BM ranged from  $-8.0$  to  $1.4\%$  and 81% of the runners profiled displayed between  $-4$  to  $0\%$   $\Delta$ BM. Nine percent (9 out of 106) of the men and 0% of the women had a %  $\Delta$ BM  $> 0$ .

The mean finishing time was computed based on 405 participants, as the finishing time for 11 participants failed to be recorded. Mean finishing times for the 42-km females, 42-km males, 84-km females and 84-km males were 358 (67), 356 (61), 668 (93) and 726 (95) min, respectively. No correlation was found between finishing time and %  $\Delta$ BM for the 42-km women category and all 84-km categories (● **Fig. 2**). Weak correlation was found for the 42-km men category.

### Discussion

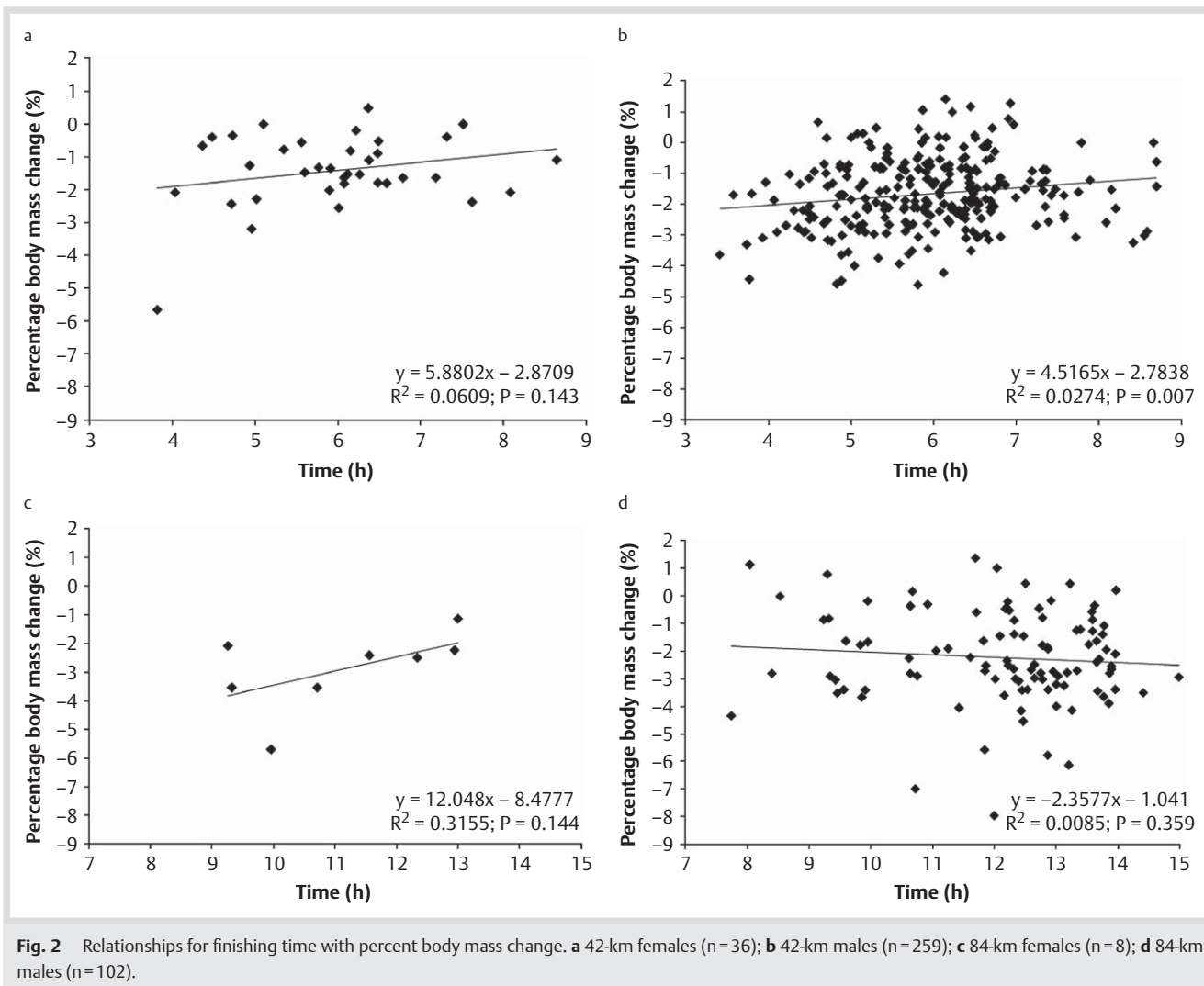
This report describes the first investigation of EAH in Asia. At the Adidas Sundown Marathon 2009 in Singapore, one runner participating in the 42-km category (1 out of 5593 who started; 1.8 out of 10000), and 2 runners participating in the 84-km category (2 out of 602 who started; 33.2 out of 10000), were diagnosed with EAH in the on-site medical tent. Exercise-associated hyponatremia was the medical condition for 38% of the 8 symptomatic runners admitted to the medical tent. A lower incidence of EAH was observed in our marathon compared with the 2000

**Table 2** Distribution of %  $\Delta$ BM.

Category	% $\Delta$ BM	No. of males	No. of females	No. of runners	Percentage of category
42-km	$> 0$	21	1	22	7%
	$\leq 0, > -2$	134	28	162	53%
	$\leq -2, > -4$	105	8	113	37%
	$\leq -4$	5	1	6	2%
84-km	$> 0$	9	0	9	8%
	$\leq 0, > -2$	38	1	39	34%
	$\leq -2, > -4$	48	6	54	47%
	$\leq -4$	11	1	12	11%

Houston Marathon, where 21 runners out of 6660 (31.8 out of 10000) were diagnosed with hyponatremia [15]. A lower incidence of EAH was also observed in our ultra-marathon compared with the 100-km 1983 American Medical Joggers Association ultramarathon race in Chicago, where 2 runners were hospitalised with hyponatremic encephalopathy out of more than 200 runners who competed [8]. One of these 2 runners placed 2<sup>nd</sup> with a race time of 8 h 36 min, before being taken to an emergency room. Similarly, our Patient 2 placed 5<sup>th</sup> with a race time of 8 h 2 min, before being admitted to the medical tent.

Exercise-associated hyponatremia is mostly a dilutional hyponatremia caused mainly by consumption of fluid in excess of urinary and sweat losses [13,17,37]. Electrolyte balance was studied during recovery in patients who developed symptomatic hyponatremia and found that there was no evidence for an excessive sodium deficit [17,37]. The present findings indicate that the proportion of those presenting to the medical tent with EAH is associated with duration of exercise, and the magnitude of the risk increases exponentially as the running distance increases  $> 42$  km. The incidence of EAH in the 84-km runners (33.2 per 10000) is  $> 18$ -fold higher than the incidence of EAH in the 42-km runners (1.8 per 10000). This exponential increase in incidence rate of EAH with the doubling of the running distance suggests that the risk of EAH increases non-linearly and at much greater magnitude than the increase in running distance. The 0.9 kg weight gain observed in Patient 2 suggests excessive fluid intake. Overdrinking occurs because of the outdated incorrect advice to consume fluids at a rate sufficient to replace all the water lost as sweat [6]. Catch phrases that promote excessive drinking, such as “drink to match sweat rates” and “drink beyond thirst”, “blanket” advice for fluid intake volumes [4], and the recommendation to drink at a rate equal to sweat rate to minimise the potential for thermal injury [6], have been widely popularised [4] and require correction. The American College of Sports Medicine (ACSM) position stand on exercise and fluid replacement in 2007 states that the goal of drinking during exercise is to prevent excessive dehydration, defined as more than 2% body weight loss, and excessive changes in electrolyte balance [30]. Athletes may use acute changes in body weight during exercise, corrected for urine losses and drink volume, to calculate sweat rates and determine individual fluid replacement needs for specific exercise and environmental conditions. While the ingestion of sports drink may reduce the extent to which the serum sodium falls, there is no empirical evidence to support the use of a sports drink in preventing EAH [30]. Volume ingestion beyond the capacity to excrete excess fluid is still paramount [1,38]. In addition to over drinking, 2 other principal factors known to cause EAH are the inadequate suppression of arginine vaso-



**Fig. 2** Relationships for finishing time with percent body mass change. **a** 42-km females (n=36); **b** 42-km males (n=259); **c** 84-km females (n=8); **d** 84-km males (n=102).

pressin (AVP) during exercise, referred to as the syndrome of inappropriate anti-diuretic hormone secretion (SIADH), and the inadequate exchange between osmotic and non-osmotic sodium stores in the body [4, 13, 27, 29, 31].

At the on-site medical tent, 3 patients were clinically diagnosed with symptomatic hyponatremia in our study. The blood sodium concentration of Patient 2 was 131 mmol/L and that of Patient 1 was 134 mmol/L, classifying these 2 cases as mild hyponatremia [16]. Patient 3 was classified as a case of severe hyponatremia, with a blood sodium concentration of 117 mmol/L. He was in a state of confusion, suggesting that his low blood sodium concentration may have induced hyponatremic encephalopathy. Despite significant dilution of his blood sodium concentration, he continued to request for fluids in the medical tent. His behaviour contradicts established findings under healthy conditions, where the physiological sensation of thirst is regulated by plasma osmolality and plasma volume [6]. We speculate that although the thirst receptors may still be functioning, cerebral edema (brain swelling) may have affected the brain's ability to respond accordingly and regulate thirst signals, compounded by a failure of the proper regulation of sodium movements between osmotic and non-osmotic stores.

Body mass changes, calculated from pre- and post-race body mass measurements, provide an insight to the fluid replacement regimes employed by athletes. In the 42-km category, 303 run-

ners (5%) were sampled to represent the 5593 who registered. In the 84-km category, 114 runners (19%) were sampled to represent the 602 who registered. Runners in the 84-km category exhibited a greater decrement in %  $\Delta$ BM compared to runners in the 42-km category. As substrate oxidation causes mass loss, the greater decrement observed in the 84-km category is expected because more substrate oxidation is required to complete the longer running distance [24]. The athlete's pre-race body mass may also include weight gain from carbohydrate and fluid loading, and from reduced training immediately before the race [14]. From previous data, we estimated that the %  $\Delta$ BM for euhydration after a 42-km run would range from 0 to -2% [18, 25], while %  $\Delta$ BM after an 84-km run would range from 0 to -4% [14, 32-36]. Data from the present study demonstrate that the majority of runners (81% for 84-km; 53% for 42-km) were within these estimated ranges for euhydration after their respective distance races. In the 42-km category, 39% of the runners displayed %  $\Delta$ BM from -2.0 to -5.7%. In the 84-km category, 11% of the runners displayed %  $\Delta$ BM from -4.0 to -8.0%. The degree of individual variation with regard to body mass change is notable: while similar amounts of fluid were made available to all the runners on race day, some runners lost 4% of body weight while a number of runners gained weight during the race. This could be either due to the individual differences in the biological



drive to drink and/or the differences in their perceptions on the correct amount of fluid to consume during races.

Whether the performances of these runners were affected by excessive loss in body mass cannot be ascertained in this study. Although these individuals are classified as dehydrated, data from Sharwood et al. [33] suggest that the absolute %  $\Delta$ BM loss at which the symptoms and signs of dehydration exhaustion prevent further exercise is influenced by both environmental and individual factors. In addition, we have previously found no association between fluid volume ingested during a 21-km running race and gastrointestinal temperature or performance [21]. Up to 6.2% body mass loss did not reveal any ill effects of dehydration in that same study. In contrast, a moderate relationship was found between the 161-km trail race finish time and percentage change in body mass ( $r=0.36$ ;  $P=0.01$ ) [20]. Conversely, those who gained weight (8% for 84-km; 7% for 42-km) in our “shorter” distance races are still of concern. We postulate that our runners who gained weight during exercise drank excessively or beyond their capacity to excrete any excess fluid. Based on the reported inverse relationship between %  $\Delta$ BM and post-race serum sodium concentration [32–34], we suggest that these athletes were at risk of incurring EAH, although unfortunately we were unable to measure blood sodium concentration in asymptomatic runners to verify this hypothesis.

Slow running or performance pace is another recognised risk factor for EAH [13], as it results in a lower sweat rate and a longer duration for drink consumption. The correlation coefficient of 0.18 between finishing time and %  $\Delta$ BM for the 42-km overall category (mean pre-race body mass 66 kg), although weak, is identical to that observed in Ironman triathletes with <70 kg body mass [32]. This negligible correlation is in contrast to an odds ratio of 7.4 (95% confidence interval, 2.9–23.1) for hyponatremia with a marathon time of >4 h compared with <3.5 h, which was observed in the 2002 Boston Marathon [1]. We suggest that environment-induced sweating was greater in our warm and humid environment compared with the cooler environment in the 2002 Boston Marathon, thereby normalising exercise intensity-induced sweating and resulting in a weaker association between finishing time and %  $\Delta$ BM.

There was a higher percentage of males who gained weight (%  $\Delta$ BM >0%) when compared to the females in both race categories. This observation is in contrast to earlier findings and does not support previous reports suggesting that females are more prone to developing EAH [1, 15]. One reason may be the small number of females profiled in this study (8 females in 84-km; 38 females in 42-km), compared with 166 females in the 2002 Boston Marathon [1]. Another reason may be that our sample consisted of mostly elite female runners. The observed shorter mean finishing time for females in the 84-km category indicates that they maintained faster speeds than their average male counterparts, and had lesser opportunities to drink. The small number of females profiled in this study and their running ability therefore may explain our contradictory findings.

We recommend that organisers of endurance events consider positioning weighing scales on-site and ensure that every participant measures his/her weight before and after their race, as change in body mass during exercise is the principle determinant of blood sodium concentration [1, 15, 27]. Cases of EAH have been reported 0.1–6 h after exercise, and the suggested cause is the large volume of water sequestered in the gastrointestinal tract that is absorbed into the blood only after cessation of exercise [3, 34]. With specific information on body mass

change, athletes will be able to proceed for medical diagnosis and early treatment if they suspect they may be at risk for EAH, even if they are currently asymptomatic. Over-provision of fluid along the race route should be discouraged and revised recommendations on fluid balance [4, 30] should be disseminated to race participants, as this has been shown to reduce the incidence of EAH in other endurance events [32, 35]. It is suggested from the results of this study that runners participating in marathons held on the Asian continent be re-educated on appropriate hydration strategies at pre-race meetings and via pre-race mailings. Local athletes and medical personnel should also be alerted to the potential dangers of EAH and hazards of overdrinking during exercise in hot and humid environments.

### Limitations

Runners who only had their body mass recorded pre- or post-race were not included in the analysis. The amount of fluid consumed during the race was not determined. Initial hydration status was not assessed before the start of the race, and some of the runners may have commenced the race already dehydrated or overhydrated. Finally, it is noteworthy that blood sodium concentrations were only measured for symptomatic patients admitted to the on-site medical tent, and therefore does not represent the exact prevalence of EAH in this race.

### Conclusion

This is the first report of EAH in Asia. Two cases of mild hyponatremia, with blood sodium concentrations 131 mmol/L and 134 mmol/L, and one case of severe hyponatremia, with blood sodium concentration 117 mmol/L, were observed. A significant proportion (8% for 84-km; 7% for 42-km) of runners over-drank, which may be attributed to an incorrect perception of hydration during exercise. This has to be rectified to minimise the incidence of EAH. It is imperative that athletes are educated on proper hydration when participating in endurance races in warm and humid environmental conditions.

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### References

- 1 Almond CS, Shin AY, Fortescue EB, Mannix RC, Wypij D, Binstadt BA, Duncan CN, Olson DP, Salerno AE, Newburger JW, Greenes DS. Hyponatremia among Runners in the Boston Marathon. *N Engl J Med* 2005; 352: 1550–1556
- 2 Arieff AI, Llach F, Massry SG. Neurological manifestations and morbidity of hyponatremia: correlation with brain water and electrolytes. *Medicine* 1976; 55: 121–129

- 3 Armstrong LE, Curtis WC, Hubbard RW, Francesconi RP, Moore R, AskeW EW. Symptomatic hyponatremia during prolonged exercise in heat. *Med Sci Sports Exerc* 1993; 25: 543–549
- 4 Beltrami FG, Hew-Butler T, Noakes TD. Drinking policies and exercise-associated hyponatremia: is anyone still promoting overdrinking? *Br J Sports Med* 2008; 42: 496–501
- 5 Casa DJ, Armstrong LE, Hillman SK, Montain SJ, Reiff RV, Rich BS, Roberts WO, Stone JA. National Athletic Trainers' Association Position Statement: fluid replacement for athletes. *J Athl Train* 2000; 35: 212–224
- 6 Convertino VA, Armstrong LE, Coyle EF, Mack GW, Sawka MN, Senay LC Jr, Sherman WM. American College of Sports Medicine position stand: exercise and fluid replacement. *Med Sci Sports Exerc* 1996; 28: i–vii
- 7 Erickson KA, Wilding P. Evaluation of a novel point-of-care system, the i-STAT portable clinical analyser. *Clin Chem* 1993; 39: 283–287
- 8 Frizzell RT, Lang GH, Lowance DC, Lathan SR. Hyponatremia and ultramarathon running. *JAMA* 1986; 255: 772–774
- 9 Goudie AM, Tunstall-Pedoe DS, Kerins M, Terris J. Exercise-associated hyponatremia after a marathon: case series. *J R Soc Med* 2006; 99: 363–367
- 10 Harriss DJ, Atkinson G. International Journal of Sports Medicine – Ethical Standards in Sport and Exercise Science Research. *Int J Sports Med* 2009; 30: 701–702
- 11 Hew-Butler TD, Almond CS, Ayus JC, Dugas J, Meeuwisse W, Noakes T, Reid S, Siegel A, Speedy D, Stuempfle K, Verbalis J, Weschler L. Consensus Statement of the 1<sup>st</sup> International Exercise-Associated Hyponatremia Consensus Development Conference, Cape Town, South Africa 2005. *Clin J Sport Med* 2005; 15: 208–213
- 12 Hew-Butler T, Anley C, Schwartz P, Noakes T. The treatment of symptomatic hyponatremia with hypertonic saline in an Ironman triathlete. *Clin J Sport Med* 2007; 17: 68–69
- 13 Hew-Butler T, Ayus JC, Kipps C, Maughan RJ, Mettler S, Meeuwisse WH, Page AJ, Reid SA, Rehrer NJ, Roberts WO, Rogers IR, Rosner MH, Siegel AJ, Speedy DB, Stuempfle KJ, Verbalis JG, Weschler LB, Wharam P. Statement of the Second International Exercise-Associated Hyponatremia Consensus Development Conference, New Zealand, 2007. *Clin J Sport Med* 2008; 18: 111–121
- 14 Hew-Butler T, Collins M, Bosch A, Sharwood K, Wilson G, Armstrong M, Jennings C, Swart J, Noakes T. Maintenance of plasma volume and serum sodium concentration despite body weight loss in Ironman triathletes. *Clin J Sport Med* 2007; 17: 116–122
- 15 Hew TD, Chorley JN, Cianca JC, Divine JG. The incidence, risk factors, and clinical manifestations of hyponatremia in marathon runners. *Clin J Sport Med* 2003; 13: 41–47
- 16 Hoorn EJ, Zietse R. Hyponatremia revisited: translating physiology to practice. *Nephron Physiol* 2008; 108: 46–59
- 17 Irving RA, Noakes TD, Buck R, van Zyl Smit R, Raine E, Godlonton J, Norman RJ. Evaluation of renal function and fluid homeostasis during recovery from exercise-induced hyponatremia. *J Appl Physiol* 1991; 70: 342–348
- 18 Kipps C, Sharma S, Tunstall Pedoe D. The incidence of exercise-associated hyponatremia in the London Marathon. *Br J Sports Med* Published Online First: 20 July 2009
- 19 Kratz A, Lewandrowski KB, Siegel AJ, Chun KY, Flood JG, Van Cott EM, Lee-Lewandrowski E. Effect of marathon running on hematologic and biochemical laboratory parameters, including cardiac markers. *Am J Clin Pathol* 2002; 118: 856–863
- 20 Lebus DK, Casazza GA, Hoffman MD, Van Loan MD. Can changes in body mass and total body water accurately predict hyponatremia after a 161-km running race? *Clin J Sport Med* 2010; 20: 193–199
- 21 Lee JKW, Nio AQX, Lim CL, Teo EY, Byrne C. Thermoregulation, pacing and fluid balance during mass participation distance running in a warm and humid environment. *Eur J Appl Physiol* 2010; 109: 887–898
- 22 Lento PH, Akuthota V. Confusion in a marathoner. *Med Sci Sports Exerc* 2002; 34: S219
- 23 Marathon victim died from drinking too much water. <http://www.dailymail.co.uk/news/article-450341/Marathon-victim-died-drinking-MUCH-water.html> Accessed 30 July 2010
- 24 Maughan RJ, Shirreffs SM, Leiper JB. Errors in the estimation of hydration status from changes in body mass. *J Sports Sci* 2007; 25: 797–804
- 25 Myhre LG, Hartung GH, Nunneley SA, Tucker DM. Plasma volume changes in middle-aged male and female subjects during marathon running. *J Appl Physiol* 1985; 59: 559–563
- 26 Noakes TD, Goodwin N, Rayner BL, Branken T, Taylor RK. Water intoxication: a possible complication during endurance exercise. *Med Sci Sports Exerc* 1985; 17: 370–375
- 27 Noakes TD, Sharwood K, Speedy D, Hew T, Reid S, Dugas J, Almond C, Wharam P, Weschler L. Three independent biological mechanisms cause exercise-associated hyponatremia: evidence from 2135 weighed competitive athletic performances. *PNAS* 2005; 102: 18550–18555
- 28 Noakes TD, Speedy DB. Case proven: exercise associated hyponatremia is due to overdrinking. So why did it take 20 years before the original evidence was accepted? *Br J Sports Med* 2006; 40: 567–572
- 29 Rosner MH, Kirven J. Exercise-associated hyponatremia. *Clin J Am Soc Nephrol* 2007; 2: 151–161
- 30 Sawka MN, Burke LM, Eichner ER, Maughan RJ, Montain SJ, Stachenfeld NS. American College of Sports Medicine position stand. Exercise and fluid replacement. *Med Sci Sports Exerc* 2007; 39: 377–390
- 31 Siegel AJ, Verbalis JG, Clement S, Mendelson JH, Mello NK, Adner M, Shirey T, Glowacki J, Lee-Lewandrowski E, Lewandrowski KB. Hyponatremia in marathon runners due to inappropriate arginine vasopressin secretion. *Am J Med* 2007; 120: 461.e11–467.e17
- 32 Sharwood K, Collins M, Goedecke J, Wilson G, Noakes T. Weight changes, sodium levels, and performance in the South African Ironman Triathlon. *Clin J Sport Med* 2002; 12: 391–399
- 33 Sharwood KA, Collins M, Goedecke JH, Wilson G, Noakes TD. Weight changes, medical complications, and performance during an Ironman triathlon. *Br J Sports Med* 2004; 38: 718–724
- 34 Speedy DB, Farris JG, Hamlin M, Gallagher PG, Campbell RG. Hyponatremia and weight changes in an ultradistance triathlon. *Clin J Sport Med* 1997; 7: 180–184
- 35 Speedy DB, Noakes TD, Rogers IR, Thompson JM, Campbell RG, Kuttner JA, Boswell DR, Wright S, Hamlin M. Hyponatremia in ultradistance triathletes. *Med Sci Sports Exerc* 1999; 31: 809–815
- 36 Speedy DB, Rogers IR, Noakes TD, Thompson JM, Guirey J, Safih S, Boswell DR. Diagnosis and prevention of hyponatremia at an ultradistance triathlon. *Clin J Sport Med* 2000; 10: 52–58
- 37 Speedy DB, Rogers IR, Noakes TD, Wright S, Thompson JM, Campbell R, Hellemans I, Kimber NE, Boswell DR, Kuttner JA, Safih S. Exercise-induced hyponatremia in ultradistance triathletes is caused by inappropriate fluid retention. *Clin J Sport Med* 2000; 10: 272–278
- 38 Twerenbold R, Knechtle B, Kakebeke TH, Eser P, Müller G, von Arx P, Knecht H. Effects of different sodium concentrations in replacement fluids during prolonged exercise in women. *Br J Sports Med* 2003; 37: 300–303
- 39 Verbalis JG. Disorders of body water homeostasis. *Best Pract Res Clin Endocrinol Metab* 2003; 17: 471–503