SCREENING AND IDENTIFICATION

Breath Alcohol Elimination Rate and Widmark Factor Derived from Breath Alcohol Concentration in Chinese and Indians in Singapore

Lie Michael George Limenta, Yee Jie Yin1, Derrick Heng2 and Edmund Jon Deoon Lee1,*

1Department of Pharmacology, Yong Loo Lin School of Medicine, National University of Singapore, Clinical Research Centre, Block MD11, 10 Medical Drive #05-09, Singapore 117597, Singapore and 2Epidemiology and Disease Control Division, Ministry of Health Singapore, 16 College Road, College of Medicine Building, Singapore 169854, Singapore

*Corresponding author: Tel.: +65-6516-3677; Fax: +65-6774-2270; E-mail: edmund_jd_lee@nuhs.edu.sg

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Abstract — Aims: To determine the breath alcohol elimination rate (AER) and Widmark factor derived from the maximum breath alcohol concentration (rpeak BrAC) in Chinese and Indians in Singapore, and to evaluate the contribution of genetic and non-genetic factors to variability of AER and rpeak BrAC. Methods: A total of 180 subjects ingested a vodka-orange juice mixture, together with a standardized meal and underwent a series of BrAC measurements. Results: Significant inter-ethnic differences in AER and rpeak BrAC were observed in females and males, respectively. Alcohol dehydrogenase 1B (ADH1B) and acetaldehyde dehydrogenase (ALDH2) genotypes were identified as significant predictors for AER among males, accounting for 8.5% (P = 0.048) and 23.4% (P < 0.001) of the variance, respectively. ADH1B genotype was identified as a significant predictor for rpeak BrAC among males, accounting for 17.1% of the variance (P = 0.001). In females, however, none of the genotypes were found to be significant predictors for breath AER, and rpeak BrAC. Conclusion: ALDH2 and/or ADH1B genotypes in males, but not in females, appear to contribute, albeit modestly, to variability in AER and rpeak BrAC. The median AER in Chinese males, Indian males, Chinese females and Indian females is 6.6 μg dL⁻¹ h⁻¹ [99% confidence interval (CI), 5.6–7.5 μg dL⁻¹ h⁻¹], 6.2 μg dL⁻¹ h⁻¹ (99% CI, 5.5–7.0 μg dL⁻¹ h⁻¹), 8.6 μg dL⁻¹ h⁻¹ (99% CI, 7.4–9.7 μg dL⁻¹ h⁻¹) and 7.4 μg dL⁻¹ h⁻¹ (99% CI, 6.2–8.4 μg dL⁻¹ h⁻¹), respectively. The median rpeak BrAC in Chinese males, Indian males, Chinese females and Indian females is 0.0229 (99% CI, 0.0216–0.0268), 0.0209 (99% CI, 0.0190–0.0237), 0.0214 (99% CI, 0.0185–0.0254) and 0.0199 (99% CI, 0.0187–0.0227), respectively.

INTRODUCTION

There has been an increase in alcohol consumption among Singaporeans over recent years. Lim et al. (2007) have compared the alcohol consumption data from three past National Health Surveys (NHS 1992, 1998 and 2004) and found increasing the prevalence of frequent (from 4.5 to 7.0%), regular (from 2.9 to 3.1%) and binge (from 5.1 to 10.0%) drinking between 1992 and 2004. Interestingly, the 1998 and 2004 NHS have suggested that both regular (i.e. frequency of alcohol consumption: >4 days a week) and binge (e.g. consumption of five or more alcoholic drinks on a single occasion) drinking are more prevalent among Chinese and Indians than Malays (Epidemiology and Disease Control Division, Ministry of Health Singapore, 1999, 2005). Moreover, alcohol consumption is also associated with road traffic accidents. In 1995, Wong et al. (2002) have reviewed the road traffic accident death occurred in Singapore over a 1-year period and found that 18.7% of road traffic accident victims tested positive for alcohol, with blood alcohol levels ranging from 13 to 292 mg dL⁻¹. The legal driving limit for breath and blood alcohol in Singapore is 35 and 80 mg dL⁻¹, respectively. Furthermore, the Singapore Police Force (SPF) reported in a media release issued on 27 November 2010, that a total of 2650 drink drivers were caught between January and November 2010 and 20% of them were involved in accidents (Public Affairs Department, 2010). Taken together, prevention and intervention efforts targeting drunk driving are considered necessary.

Although there is no safe minimum alcohol intake limit for drinking and driving, the provision of information, on the amount of alcohol intake needed to reach the legal blood/breath alcohol limit, could change public knowledge and attitudes towards drunk driving. The Widmark formula

\[ r_0 = A \times 100/W \times C_0, \]

where \( r_0 \) is the Widmark factor, \( A \) the amount of alcohol consumed in grams, \( W \) the body weight in kilograms and \( C_0 \) the theoretical initial blood alcohol concentration (BAC) at time zero in mg dL⁻¹ has been widely used to estimate the theoretical maximum alcohol level attained after consumption of a particular quantity of alcohol with knowledge of the subject’s body weight and gender. The average value of Widmark factor \( r_0 \), however, is derived from the blood alcohol kinetic data of Caucasian subjects in the fasting state and therefore may not be applicable to other ethnic groups and social drinking. A study by Tam et al. (2005) reported slightly higher \( r_0 \) values for local Chinese in Hong Kong (males: 0.71; females: 0.62) than those reported by Widmark for Caucasians (males: 0.69; females: 0.55). They have further suggested the use of the practical Widmark factor \( r_{peak} \), which is derived from the measured maximum concentration \( C_{max} \) of blood alcohol, as alcohol distribution, metabolism and elimination processes may occur concomitantly with its absorption process. The statutory 2300:1 blood-to-breath relationship has not been clinically validated in our population, and the BAC/breath alcohol concentration (BrAC) conversion factor has been shown to be dependent on BrAC (Haffner et al., 2003; Pavlic et al., 2006). Since BrACs were measured in the present study, the \( r_{peak} \) formula was modified by using \( C_{max} \) of breath alcohol instead of converted equivalent blood alcohol.

Knowledge of the alcohol elimination rate (AER), together with \( C_{max} \), is indeed essential in estimating body alcohol level at a particular time. Moreover, inter-ethnic and inter-individual differences in the AER have been reported and genetic polymorphisms of alcohol-metabolizing enzymes, such as alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH) and cytochrome P450 2E1 (CYP2E1), have been suggested to contribute to the observed variability.
(Stephens et al., 1994; Norberg et al., 2003; Eng et al., 2007; Chen et al., 2009). However, only a few studies have evaluated the effect of combined alcohol-metabolizing enzyme genotypes on AER thus far (Yoshihara et al., 2000). Likewise, there have been a very limited number of studies evaluating the effect of alcohol-metabolizing enzyme genotypes on the variability of Widmark factor. A study by Mizoi et al. (1985) has provided evidence of higher Widmark factor \( r_0 \) values in Japanese healthy males with \( ALDH2 \)-deficient genotype.

The present study was undertaken to determine the breath AER and the Widmark factor derived from maximum BrAC \( (r_{peak} \text{ BrAC}) \) in Chinese and Indians in Singapore. The effects of genetic factors [i.e. single nucleotide polymorphisms (SNPs) in \( ADH1B \) (Arg48His), \( ALDH2 \) (Glu504Lys) and \( CYP2E1 \) promoter (c.-1293G>C and c.-1053C>T)] and non-genetic factors (i.e. amount of alcohol consumed, age, body weight, and height) in explaining the variability of breath AER and \( r_{peak} \text{ BrAC} \) were also evaluated.

MATERIALS AND METHODS

Subjects and conditions

A total of 180 subjects (90 Chinese and 90 Indians; 45 males and 45 females from each ethnic group) participated in this study. The study protocol was evaluated and approved by the Institutional Review Board of the Changi General Hospital, Singapore. All subjects underwent screening assessment tests, including progesterone (females only) and liver function tests prior to the study to confirm the subject’s health status. The genetic sample from the subjects taken during screening period was analyzed for SNP variants in health status. The genetic sample from the subjects taken during screening period was analyzed for SNP variants in health status. The genetic sample from the subjects taken during screening period was analyzed for SNP variants in health status.

BrAC analysis

BrACs were measured by calibrated Alcolizer LE (Alcolizer Technology, Cleveland, QLD) within 30 min before the first drink (time 0), and at 1.5, 2, 2.5, 3, 3.25, 3.5, 3.75, 4, 4.25, 4.5, 4.75, 5 and 6 h after the first drink. Alcolizer LE is used by the SPF for legally valid breath alcohol measurements in ring-fencing operation. For a valid result, two independent breath samples were obtained and the time interval between two successive breath alcohol measurements was <3 min. After an overnight fast, male and female subjects ingested a mixture of vodka and orange juice, containing 54 and 36 g of ethanol, respectively over an hour, together with a standardized light meal to mimic social drinking. The alcohol intake was adjusted for gender in order to avoid concentration-related adverse effects, particularly vomiting, as females have been known to achieve higher peak BrAC than males after ingesting an equivalent dose (Pavlic et al., 2007).

AER and \( r_{peak} \text{ BrAC} \) determinations

BrAC-time profiles were plotted for each subject. The mean of each duplicate measurement was taken as the BrAC at that time point. The maximum BrAC \( (C_{\text{max}}) \) values and time to reach the \( C_{\text{max}} \) (\( t_{\text{max}} \)) values were determined by observation of the individual concentration-time data. Breath AER was calculated by linear least square regression of the pseudolinear portion of the BrAC-time curve. The Widmark factor \( r_{peak} \text{ BrAC} \) was calculated using the following formula:

\[
r_{\text{peak BrAC}} = \frac{A}{W \times C_{\text{max}}}
\]

where \( A \) is the amount of alcohol consumed in grams, \( W \) the body weight in kilograms and \( C_{\text{max}} \) the maximum BrAC in \( \mu g \text{ dl}^{-1} \).

PCR and sequence analysis

The fragments of SNPs of interest were generated using the primer sequences shown in Table 1. The amplifications were performed in a total volume of 30 \( \mu \)l containing 1 \( \times \) Master Mix (Promega, Madison, WI, USA), 0.4 mM of both forward and reverse primer (Sigma Proligo, Singapore) and 60 ng of DNA. PCR conditions were as follows: pre-denaturation at 95°C for 5 min, followed by 39 cycles of denaturation at 95°C for 1 min, annealing at temperature shown in Table 1 for 1 min and extension at 72°C for 1 min and a final extension at 72°C for 10 min.

PCR products were sequenced using the Big-Dye Terminator v3.1 Cycle Sequencing Kit and run on the automated ABI Prism Model 3100 Avant Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). The sequences were analyzed with Chromas (Tecelysium software).

Statistical analysis

Normal distribution of the continuous data was evaluated by the Shapiro–Wilk test and consequently parametric tests and non-parametric tests were applied when appropriate. Data are expressed as mean (±SD) for normally distributed continuous variables and median (minimum–maximum) for normally distributed continuous variables. Since gender has been known to have a measurable influence on the alcohol kinetics, the statistical analyses were performed separately for males and females. Statistical comparisons of the studied parameters between the two groups were performed by using the parametric independent t-test or the non-parametric Mann–Whitney U-test as appropriate.

Multiple linear regression analysis was used to investigate the following variables as possible explanatory (independent) variables: age, weight, height, genotypes (\( CYP2E1, ADH1B \) and \( ALDH2 \)), ethnicity and amount of alcohol consumed, in relation to the following dependent variables: log-

<table>
<thead>
<tr>
<th>SNPs</th>
<th>Primer sequences</th>
<th>Annealing temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>( CYP2E1 ):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c.-1293G&gt;C</td>
<td>Forward primer: 5'</td>
<td>50</td>
</tr>
<tr>
<td>c.-1053C&gt;T</td>
<td>Reverse primer: 5'</td>
<td></td>
</tr>
<tr>
<td>Arg48His</td>
<td>Forward primer: 5'</td>
<td>50</td>
</tr>
<tr>
<td>ADH1B</td>
<td>Reverse primer: 5'</td>
<td></td>
</tr>
<tr>
<td>Glu504Lys</td>
<td>Forward primer: 5'</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Reverse primer: 5'</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Primer sequences
transformed breath AER, and negative reciprocal of $r_{\text{peak BrAC}}$. Variable selection was performed using an automated backward stepwise regression with a $P$-value for entry of 0.05 and a $P$-value for removal of 0.1, followed by a forward stepwise regression to determine the best independent predictors of the dependent variable. General linear model (GLM) univariate was applied if one of the selected explanatory variables was a categorical variable with more than two categories (e.g. $ADH1B$ genotype).

The $\chi^2$ test was applied to test the deviation of allele and genotype frequency distributions from Hardy–Weinberg equilibrium. Fisher’s exact test was applied to compare the allele frequencies between the vomiting and non-vomiting groups. Statistical analyses were performed with SPSS software (version 19, SPSS, Chicago, IL, USA). $P < 0.05$ was considered significant.

RESULTS

The kinetic profiles of alcohol are available for 180 subjects. Twenty-three Chinese (14 males and 9 females) and 3 Indians (1 male and 2 females) experienced alcohol-induced vomiting during the study. Data from individuals who vomited were excluded in order to prevent bias arising from incomplete alcohol ingestion. Chinese males had significantly higher median age (35 vs. 28 years, $P = 0.045$), lower median alanine transaminase levels (20 vs. 28 U l$^{-1}$, $P = 0.007$) and lower median aspartate transaminase levels (21 vs. 25 U l$^{-1}$, $P = 0.002$) than did Indian males. Chinese females had significantly lower mean weight (55 vs. 63 kg, $P < 0.001$), lower mean height (1.57 vs. 1.60 m, $P = 0.047$) and higher median serum albumin levels (42 vs. 39 g l$^{-1}$, $P = 0.002$) compared with Indian females (Table 2).

The BrAC-time profiles in males and females are shown in Fig. 1a and b, respectively, and their kinetic parameters are shown in Table 3. The mean alcohol intake per kilogram of body weight was comparable among males. Since Indian females were significantly heavier than Chinese females, the average amount of alcohol consumed per kilogram of body weight in Chinese females was 15% higher than that in Indian females ($P < 0.001$). The breath alcohol $C_{\text{max}}$ was comparable between ethnic Chinese and ethnic Indians in both males and females. When normalized for the alcohol intake per kilogram of body weight, Indian males, however, had a 13% higher mean $C_{\text{max}}$ than did Chinese males ($P = 0.007$). In most of the subjects, the $C_{\text{max}}$ was reached within 1.5 h after the first sip. Eight males (2 Chinese and 6 Indians) and 18 females (7 Chinese and 11 Indians) reached $C_{\text{max}}$ between 2 and 3 h after the first sip. The median breath AER was comparable among males. On the other hand, Chinese females were found to eliminate alcohol 16% faster than Indian females ($P = 0.005$). No significant difference was observed in median $r_{\text{peak BrAC}}$ value among females. Chinese males had a 9.5% higher median $r_{\text{peak BrAC}}$ than did Indian males ($P = 0.011$).

The frequency distribution of $ALDH2$ and $ADH1B$ genotypes were in Hardy–Weinberg equilibrium in both ethnic Chinese and ethnic Indians. The frequencies of the $ALDH2$ GG, GA and AA genotypes in ethnic Chinese were 76, 24 and 0%, respectively, and those in ethnic Indians were 100, 0 and 0%, respectively. The frequencies of the $ADH1B$ GG, GA and AA genotypes in ethnic Chinese were 12, 43 and 45%, respectively, and those in ethnic Indians were 89, 10 and 1%, respectively. The frequency distribution of $CYP2E1$ c.-1293G>C and c.-1053C>T promoter polymorphisms was significantly deviated from Hardy–Weinberg equilibrium in ethnic Indians, but not in ethnic Chinese. The frequencies of the $CYP2E1$ (c.-1293G>C) GG, GC and CC genotypes in ethnic Chinese were 60, 31 and 9%, respectively, in ethnic Chinese and 64, 32 and 4%, respectively, in ethnic Indians. The frequencies of the $CYP2E1$ (c.-1053C>T) TT, CT and CC genotypes in ethnic Chinese were 45, 52 and 3%, respectively, in ethnic Chinese and 51, 48 and 1%, respectively, in ethnic Indians.

Table 2. Demographic and clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chinese</td>
<td>Indian</td>
<td>Chinese</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>31</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35 (21–62)</td>
<td>28 (21–59)$^a$</td>
<td>28 (21–58)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 (11)</td>
<td>76 (12)</td>
<td>55 (8)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.73 (0.06)</td>
<td>1.73 (0.08)</td>
<td>1.57 (0.05)</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>43 (13–49)</td>
<td>42 (37–49)</td>
<td>42 (37–48)</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>20 (12–74)</td>
<td>28 (13–126)$^a$</td>
<td>16 (8–46)</td>
</tr>
<tr>
<td>AST (U/l)</td>
<td>21 (16–43)</td>
<td>25 (16–88)$^a$</td>
<td>21 (14–30)</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD or median (minimum–maximum); ALT, alanine transaminase; AST, aspartate transaminase.

$^a$Significant difference from Chinese males ($P < 0.05$).

$^b$Significant difference from Chinese females ($P < 0.05$).

Fig. 1. Time course of breath alcohol concentration in males (a) and females (b). Data are presented as mean ± SD.
Table 3. Breath alcohol kinetic parameters

<table>
<thead>
<tr>
<th>Alcohol intake (g kg⁻¹)</th>
<th>Chinese</th>
<th>Indian</th>
<th>Females</th>
<th>Chinese</th>
<th>Indian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (µg dl⁻¹)</td>
<td>0.78 (0.13)</td>
<td>0.73 (0.11)</td>
<td>0.68 (0.11)</td>
<td>0.59 (0.10)</td>
<td></td>
</tr>
<tr>
<td>tmax (h)</td>
<td>32.6 (8.5)</td>
<td>35.0 (8.7)</td>
<td>32.1 (8.3)</td>
<td>29.3 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Breath AER (µg dl⁻¹ h⁻¹)</td>
<td>6.6 (4.1–10.2)</td>
<td>6.2 (4.0–10.5)</td>
<td>8.6 (1.7)</td>
<td>7.5 (1.8)</td>
<td></td>
</tr>
<tr>
<td>Alcohol intake-normalized Cmax (µg dl⁻¹)</td>
<td>42.0 (8.4)</td>
<td>47.6 (8.7)</td>
<td>47.6 (10.4)</td>
<td>49.3 (9.8)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as mean (±SD) or median (minimum–maximum); BrAC, breath alcohol concentration; Cmax, observed maximum BrAC; tmax, time to reach Cmax; AER, alcohol elimination rate; rpeak BrAC, Cmax-derived Widmark factor.

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Table 4. Multiple linear regression and GLMs

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>F-value/standardized β coefficient</th>
<th>Partial Eta squared/adjusted R² value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males Breath AER</td>
<td>ADH1B</td>
<td>3.182</td>
<td>0.085</td>
<td>0.048</td>
</tr>
<tr>
<td></td>
<td>ADH2</td>
<td>21.051</td>
<td>0.234</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>ADH1B*ALDH2</td>
<td>1.530</td>
<td>0.022</td>
<td>0.220</td>
</tr>
<tr>
<td></td>
<td>ALDH2</td>
<td>7.433</td>
<td>0.171</td>
<td>0.001</td>
</tr>
<tr>
<td>Females Breath AER</td>
<td>Albumin</td>
<td>0.413</td>
<td>0.159</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>rpeak BrAC</td>
<td>0.021</td>
<td>0.020</td>
<td>0.001</td>
</tr>
</tbody>
</table>

AER, alcohol elimination rate; BrAC, breath alcohol concentration; Cmax, observed maximum BrAC; rpeak BrAC, Cmax-derived Widmark factor; ADH1B, alcohol dehydrogenase 1B; ALDH2, acetaldehyde dehydrogenase; NA, not available.

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Chinese and those in ethnic Indians were 96, 3 and 1%, respectively. The frequencies of the CYP2E1 (c.-1053C>T) CC, CT and TT genotypes in ethnic Chinese were 57, 34 and 9%, respectively, and those in ethnic Indians were 94, 5 and 1%, respectively. In ethnic Chinese, the frequency of the ALDH2 A allele (ALDH2*1) was significantly higher in the vomiting group than in the non-vomiting group (50 vs. 12%, P < 0.001). Likewise in the ethnic Indians, although the number of subjects in the vomiting group was small (n = 3), the ALDH2 A allele frequency was higher than that in the non-vomiting group (33 vs. 0%, P = 0.001). No significant difference was observed for the frequency distribution of ADH1B and CYP2E1 promoter alleles between the vomiting and the non-vomiting groups in either ethnic group (data not shown).

In a GLM analysis with amount of alcohol consumed as covariate, ADH1B and ALDH2 genotypes were identified as significant predictors for breath AER among males, accounting for 8.5% (P = 0.048) and 23.4% (P < 0.001) of the variance, respectively; no interaction between ADH1B and ALDH2 genotypes was found (P = 0.220; Table 4). ADH1B genotype was identified as a significant predictor for rpeak BrAC among males, accounting for 17.1% of the variance (P = 0.001). In females, however, none of the genotypes were found to be significant predictors for breath AER, and rpeak BrAC (Table 3).

DISCUSSION

We observed a 2.6-fold variability for males and a 3.2-fold variability for females in breath AER. The ranges of the determined breath AER in this study (male, 4.0–10.5 µg dl⁻¹ h⁻¹; female, 4.4–14.0 µg dl⁻¹ h⁻¹) were quite similar to those reported by Tam et al. (2006) in Hong Kong Chinese (male, 4.1–10.3 µg dl⁻¹ h⁻¹; female, 4.8–16.1 µg dl⁻¹ h⁻¹). We, as with previously published studies (Thomasson, 2000; Baraona et al., 2001; Pavlic et al., 2007), also observed significant gender difference in median breath AER (male, 6.5 µg dl⁻¹ h⁻¹; female, 7.8 µg dl⁻¹ h⁻¹; P < 0.05) although this result must be interpreted with caution due to the difference in dosing regimen. Interestingly, significant inter-ethnic difference in breath AER was observed only in females. The reason for this difference is unclear. The amount of alcohol consumed has been shown to have no significant effect on breath AER (Friel et al., 1999; Tam et al., 2006). Furthermore, Li et al. (2000) have suggested that liver size is the major determinant of gender and ethnic differences in AER; they have found that black Americans have lower AERs than white Americans following oral administration of equivalent alcohol dose. They have also reviewed the autopsy reports of eligible accidental death victims and found that the liver weight per kilogram body weight is the only significant predictor for breath AER (Friel et al., 1999; Tam et al., 1999; Tam et al., 1999). The effects of liver weight or volume on AER in Asian, however, are unknown and remain to be investigated. Furthermore, multiple regression analysis identified serum albumin level as the only significant predictor for breath AER among females, although accounting for a modest 15.9% of the variance (P < 0.001). Yet, there have been very few studies that examine the relationship between AER and serum albumin level. A study in alcoholics and control subjects by Ueno et al. (1996) has reported no correlation between AER and serum albumin although the majority (>95%) of the subjects
in their study were males. No statistically significant ethnic difference in breath AER was found among males in our study. We further found that ADH2 genotype is a significant and a stronger predictor for breath AER than ADH1B genotype among males (23.4 vs. 8.5% of the variance, Table 3). This is in agreement with the findings of Hesselbrock et al. (2005), who have reported that male, but not female, subjects with ALDH2*1/*2 genotype show significantly lower AERs than those with ALDH2*1/*1 genotype; they have also shown no significant differences in lean body mass-adjusted AER among ADH1B genotypes in either males or females. Similar to our findings, Neumark et al. (2004) have reported that ADH1B allele accounts for only 8.5% of the breath AER variance in male Jews. Also noteworthy is the higher frequency of ADH2 A allele in the vomiting group may suggest that excluding vomiters from the analysis may introduce potential inadvertent bias toward underestimation of genotype effects, although this possibility cannot be ruled out.

The Widmark factor \( r_{\text{peak BrAC}} \) values showed 4.2-fold variability for males and 3.1-fold variability for females. When BAC/BrAC conversion factor of 2300 was applied, the range of determined \( r_{\text{peak}} \) in this study (0.57–2.69) was quite similar to that reported by Tam et al. (2005) in Hong Kong Chinese (0.48–2.05). Also, we observed significant gender differences in \( r_{\text{peak}} \) (male, 0.962; female, 0.889; \( P < 0.05 \)), providing further support for the previously reported gender differences in \( r_{\text{peak}} \) (Tam et al., 2005). It is noteworthy that significant inter-ethnic difference in \( r_{\text{peak BrAC}} \) was observed only in males. Likewise, when normalized for the alcohol intake per kilogram of body weight, the average \( C_{\text{max}} \) was significantly higher in Indian males than in Chinese males (\( P = 0.007 \)). ADH1B genotype was shown to explain 17.1% of the \( r_{\text{peak BrAC}} \) variability in males though it could not explain the inter-ethnic difference. The rate of alcohol absorption has been shown to be dependent on gastric emptying and therefore may be partially responsible for the observed inter-ethnic difference (Holt, 1981). Schwartz et al. (1996) have demonstrated that the gastric emptying rate of beer in Mexican-Americans is significantly faster than that in non-Hispanic whites. Further studies are necessary to validate this hypothesis in Asian populations.

Based on the first percentile of the distribution of body weight from the 2010 NHS (i.e. Chinese males, 45.6 kg; Indian males, 48.7 kg; Chinese females, 39.4 kg; Indian females, 39.5 kg) and the lower 99% confidence limit for Widmark factor \( r_{\text{peak BrAC}} \) determined in this study, then the intake of alcohol should not exceed 34.5 g for Chinese males, 23.4 g for Indian males, 25.5 g for Chinese females and 25.8 g for Indian females, and the individuals should not drive within 3 h as they are more likely to reach the legal breath alcohol limit. This amount of alcohol translates to approximately 2.5–2.6 cans (330 ml) of beer (5% v/v) or 2.7–2.9 glasses (125 ml) of wine (12% v/v) for males, and two cans of beer (5% v/v) or 2.1–2.2 glasses of wine (12% v/v) for females. Indeed, it is important to note that there is no safe minimum alcohol intake limit for drinking and driving since driving-related skills have been shown to be affected even at low blood alcohol levels (Koelega, 1995; Moskowitz et al., 2000). A meta-analysis study by Taylor et al. (2010) have reported an odds ratio of 2.2 for motor vehicle accident injury even at a generally accepted moderate dose (24 g of alcohol) although the gender effects could not be analyzed since most of the studies included in their analysis only reported combined estimates for males and females. Moreover, Liu and Ho (2010) have recently shown no significant difference in driver’s driving behaviors and cognitive task performance between drunk and post-alcohol (where BAC = 0%) sessions; they have therefore suggested that post-alcohol impairment exists and adversely affects driving skills, vigilance and depth perception. It is worth mentioning that several Asian countries, such as China, Hong Kong, India, Japan and Thailand, have adopted lower legal blood alcohol limits than Singapore, ranging from 20 to 50 mg dl⁻¹. Reducing the legal alcohol limit has been shown to be an effective strategy in reducing alcohol-involved motor vehicle crashes (Fell and Voas, 2006; Desapriya et al., 2007). Further studies are necessary to evaluate whether the current legal alcohol limit is generously permissive to drunk driving in the Singaporean population.

**CONCLUSION**

The median breath AERs in Chinese males, Indian males, Chinese females and Indian females are 6.6 μg dl⁻¹ h⁻¹ [99% confidence interval (CI), 5.6–7.5 μg dl⁻¹ h⁻¹], 6.2 μg dl⁻¹ h⁻¹ (99% CI, 5.5–7.0 μg dl⁻¹ h⁻¹), 8.6 μg dl⁻¹ h⁻¹ (99% CI, 7.4–9.7 μg dl⁻¹ h⁻¹) and 7.4 (99% CI, 6.2–8.4 μg dl⁻¹ h⁻¹), respectively. The Widmark’s median \( r_{\text{peak BrAC}} \) factors in Chinese males, Indian males, Chinese females and Indian females are 0.0229 (99% CI, 0.0216–0.0268), 0.0209 (99% CI, 0.0190–0.0237), 0.0214 (99% CI, 0.0185–0.0254) and 0.0199 (99% CI, 0.0187–0.0227), respectively. The Widmark’s median \( r_{\text{peak BrAC}} \) factors in Chinese males, Indian males, Chinese females and Indian females are 0.0229 (99% CI, 0.0216–0.0268), 0.0209 (99% CI, 0.0190–0.0237), 0.0214 (99% CI, 0.0185–0.0254) and 0.0199 (99% CI, 0.0187–0.0227), respectively. ALDH2 and/or ADH1B genotypes in males, but not in females, appear to contribute, albeit modestly, to variability in breath AER and \( r_{\text{peak BrAC}} \).

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**REFERENCES**


Fell JC, Voas RB. (2006) The effectiveness of reducing illegal blood alcohol concentration (BAC) limits for driving: evidence for lowering the limit to 0.05 BAC. *J Safety Res* 37:233–43.


