

Abstract

National distribution of rs671 (ALDH2) genotypes and the effect of alcohol on chronic disease in each genotype

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Ingested alcohol is oxidized to acetaldehyde through the primary metabolic process, and this acetaldehyde is finally oxidized to acetic acid by acetaldehyde dehydrogenase (ALDH2), which plays a very important role in alcohol metabolism. In a large cohort population, the frequency of each genotype of rs671 (ALDH2), drinking status, and the prevalence of hypertension and diabetes according to the amount of alcohol in each genotype were analyzed.

To analyze the frequency of each genotype of rs671 (ALDH2) in Korean people, genetic information produced by the Korea Biobank Array (KBA) for a large-scale cohort of the Genomic Epidemiology Project (KoGES) and human resources distributed from the National Health and Nutrition Examination Survey were used. As a result, 1,859 out of total 79,389 subjects were identified as carrying AA genotype (homozygous) and 21,256 were identified as carrying GA genotype (heterozygous). Thus, 29.1% of the total subjects were identified as carrying minor allele types (GA+AA) of rs671 (ALDH2), which are very vulnerable to alcohol drinking. When this study analyzed the drinking status of the minor allele types (GA+AA) of rs671 (ALDH2) in the large population, which was comprised of 53,020 people in the urban cohort, 3,636 people in the rural cohort, and 5,011 people in the community cohort, 75.3% were non-drinkers, 14.2% were low-level drinkers, 8.6% were middle-level drinkers, and 1.9% were high-level drinkers. In the case of major GG type (Reference allele) of rs671 (ALDH2), 30.7% had hypertension and 9.0% had diabetes. However, in the high-level drinkers carrying major GG type, 40.9% had hypertension and 12.9% had diabetes. On the other hand, in the case of minor allele types (GA+AA) of rs671 (ALDH2), 28.4% of non-drinkers had hypertension and 8.5% had diabetes. However, in the high-level drinkers carrying minor allele types, 29.5% had hypertension and 5.2% had diabetes, showing a slightly lower percentage than those of major allele (GG) of rs671 (ALDH2).

This is the first report to analyze the frequency of each genotype of rs671 (ALDH2) in a large-scale Korean population, drinking status of minor allele-carriers and the effects of alcohol drinking on hypertension and diabetes in each genotype. As a cross-sectional study, this study has some limitation in that it could not analyze the effects of long-term alcohol drinking such as changes in clinical characteristics and the prevalence of hypertension and diabetes. To get more statistical significance and reliable results, it is necessary to carry out prospective or retrospective observational studies in a different large-scale population.

Keywords: rs671 (ALDH2), GG genotype, AA genotype, GA genotype, prevalence

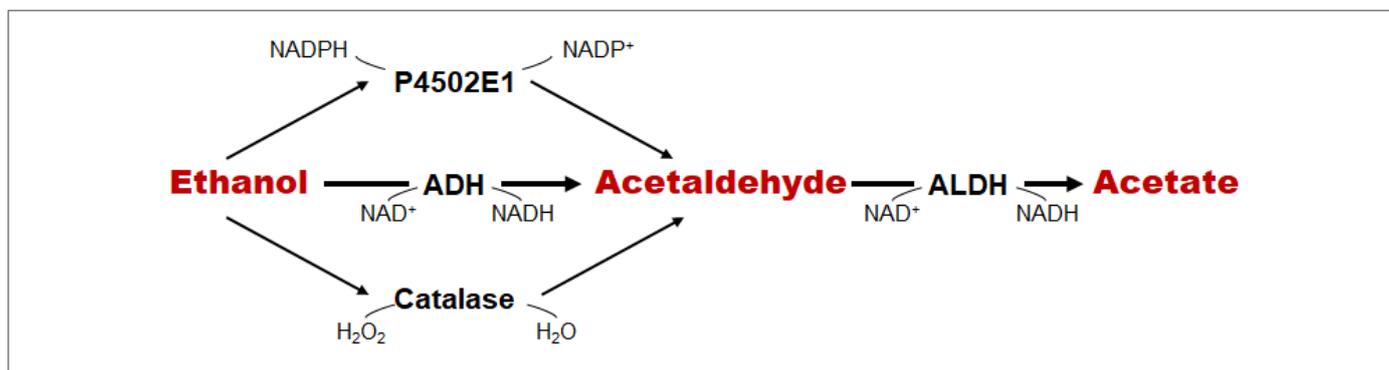


Figure 1. Alcohol metabolism

Table 1. ALDH2 rs671 genetic variant distribution according to genotyping production methods

ALDH2 rs671	Korea Biobank Array (KBA)			TaqMan	Total
	HEXA	CAVAS	KARE	KNHANES	
	n=55,943	n=3,936	n=5,492	n=14,018	n=79,389
GG	39,550 (70.7)	2,864 (72.8)	3,899 (71.0)	9,961 (71.1)	56,274 (70.9)
GA	15,108 (27.0)	983 (25.0)	1,452 (26.4)	3,713 (26.5)	21,256 (26.8)
AA	1,285 (2.3)	89 (2.7)	141 (2.6)	344 (2.5)	1,859 (2.3)

HEXA, Health examines cohort; CAVAS, Cardiovascular disease association study; KARE, Korean association resource; KNHANES, Korea national health and nutrition survey

Table 2. General characteristics of Korean Genome and Epidemiology Study (KoGES)

	HEXA (n=53,020)	CAVAS (n=3,636)	KARE (n=5,011)	p-value
Sex				<0.0001
Men	17,578 (33.2)	1,322 (36.4)	2,291 (45.7)	
Women	35,442 (66.9)	2,314 (63.6)	2,720 (54.3)	
Age	53.7±8.0	60.1±8.9	51.4±8.5	<0.0001
Systolic blood pressure	122.4±14.8	127.7±18.0	120.9±18.0	<0.0001
Diastolic blood pressure	75.7±9.7	80.5±11.3	80.1±11.2	<0.0001
Fasting glucose	94.9±19.4	100.5±24.2	92.3±21.4	<0.0001
HDL-cholesterol	53.9±13.1	46.2±11.4	49.5±11.5	<0.0001
Triglycerides	125.0±86.0	154.7±101.1	152.4±110.6	<0.0001
ADLH2				0.1337
GG	37,236 (70.2)	2,619 (72.0)	3,534 (70.5)	
GA	14,525 (27.4)	934 (25.7)	1,345 (26.8)	
AA	1,259 (2.4)	83 (2.3)	132 (2.6)	
Drinking				<0.0001
Non-drinking	28,819 (54.4)	2,063 (56.7)	2,483 (49.6)	
Low	10,540 (19.9)	615 (16.9)	914 (18.2)	
Intermediate	9,367 (17.7)	570 (15.7)	1,025 (20.5)	
High	4,294 (8.1)	388 (10.7)	589 (11.8)	
Hypertension	15,201 (28.7)	2,161 (59.5)	1,530 (30.5)	<0.0001
Type 2 diabetes	4,439 (8.6)	532 (14.6)	406 (8.1)	<0.0001
Amount of alcohol*	15.8±32.1	22.4±35.9	20.3±27.5	<0.0001

*Excluding non-drinking

HEXA, Health examines cohort; CAVAS, Cardiovascular disease association study; KARE, Korean association resource

Table 3. General and clinical characteristics according to rs671 (ALDH2)

	rs671(ALDH2)			p-value
	GG	GA	AA	
<HEXA>				
Age	53.6±7.9	53.9±8.0	54.0±8.1	<0.0001
Systolic blood pressure	122.7±14.9	121.5±14.4	122.1±14.4	<0.0001
Diastolic blood pressure	76.0±9.8	75.1±9.5	75.2±9.5	<0.0001
Fasting glucose	95.3±19.8	93.8±18.5	93.7±16.0	<0.0001
HDL-cholesterol	54.4±13.3	52.7±12.6	51.7±12.2	<0.0001
Triglycerides	126.1±89.2	122.2±77.9	123.7±76.2	<0.0001
Alcohol				<0.0001
Non-drinking	46,960 (45.6)	10,663 (73.4)	1,196 (95.0)	
Low	8,261 (22.2)	2,228 (15.3)	51 (4.1)	
Intermediate	8,011 (21.5)	1,345 (9.3)	11 (0.9)	
High	4,004 (10.8)	289 (2.0)	1 (0.1)	
<CAVAS>				
Age	59.8±8.9	60.8±8.7	61.9±9.2	0.0032
Systolic blood pressure	127.9±17.9	127.2±18.3	125.4±17.8	0.2817
Diastolic blood pressure	80.7±11.3	80.0±11.2	79.7±11.9	0.1545
Fasting glucose	101.3±24.8	98.5±22.6	99.3±22.4	0.0112
HDL-cholesterol	46.4±11.4	45.7±11.4	45.1±10.4	0.1930
Triglycerides	158.5±106.0	144.6±87.6	151.0±73.4	0.0014
Alcohol				<0.0001
Non-drinking	1,242 (47.2)	738 (79.0)	83 (100.0)	
Low	509 (19.4)	106 (11.4)	-	
Intermediate	502 (19.2)	68 (7.3)	-	
High	366 (14.0)	22 (2.4)	-	
<KARE>				
Age	51.3±8.4	51.8±8.6	51.3±8.2	0.1743
Systolic blood pressure	121.2±18.1	120.0±17.6	119.8±18.8	0.1023
Diastolic blood pressure	80.3±11.3	79.4±11.1	79.8±10.3	0.0407
Fasting glucose	93.0±22.3	90.6±18.7	89.4±21.0	0.0007
HDL-cholesterol	50.1±11.7	48.0±10.8	49.1±12.0	<0.0001
Triglycerides	155.8±113.8	146.1±104.5	126.9±66.8	<0.0001
Alcohol				
Non-drinking	1,407 (39.8)	947 (70.4)	129 (97.7)	
Low	700 (19.8)	212 (15.8)	2 (1.5)	
Intermediate	879 (24.9)	145 (10.8)	1 (0.8)	
High	548 (15.5)	41 (3.1)	-	

HEXA, Health examines cohort; CAVAS, Cardiovascular disease association study; KARE, Korean association resource

Table 4. General and clinical characteristics according to alcohol consumption

	Non-drinker	Low	Intermediate	High	p-value
<HEXA>					
Age	54.6±7.8	52.2±7.9	53.2±8.2	52.6±7.8	<0.0001
Systolic blood pressure	121.5±14.9	120.9±14.4	124.7±14.3	126.5±14.6	<0.0001
Diastolic blood pressure	74.8±9.6	74.9±9.6	77.9±9.6	79.2±9.9	<0.0001
Fasting glucose	93.7±18.9	93.3±17.5	97.6±52.7	100.7±23.6	<0.0001
HDL-cholesterol	53.7±12.8	54.9±13.4	52.7±13.1	54.8±14.3	<0.0001
Triglycerides	118.4±74.6	114.7±74.6	139.9±99.6	161.6±127.9	<0.0001
<CAVAS>					
Age	60.7±8.8	59.1±8.8	59.5±9.1	59.9±8.8	0.0002
Systolic blood pressure	126.7±17.9	127.5±17.8	128.7±17.6	131.9±18.9	<0.0001
Diastolic blood pressure	79.5±11.2	80.6±10.7	82.4±11.7	83.1±11.4	<0.0001
Fasting glucose	98.6±23.6	101.8±24.3	101.9±20.2	106.7±30.7	<0.0001
HDL-cholesterol	45.7±10.8	45.9±11.5	46.0±11.6	49.0±13.6	<0.0001
Triglycerides	147.0±85.4	147.6±95.5	167.1±116.9	189.2±144.0	<0.0001
<KARE>					
Age	52.9±8.7	50.3±8.1	50.0±8.0	49.4±7.9	<0.0001
Systolic blood pressure	121.4±18.9	118.2±17.5	120.6±16.5	123.2±17.2	<0.0001
Diastolic blood pressure	79.3±11.3	78.7±10.7	81.4±10.5	83.2±11.8	<0.0001
Fasting glucose	90.7±19.4	90.0±17.5	94.3±24.6	98.9±26.4	<0.0001
HDL-cholesterol	49.0±11.2	50.1±11.8	48.9±11.3	51.4±12.5	<0.0001
Triglycerides	142.2±96.1	137.8±104.8	171.4±124.1	185.2±137.1	<0.0001

HEXA, Health examines cohort; CAVAS, Cardiovascular disease association study; KARE, Korean association resource

Table 5. General and clinical characteristics according to alcohol consumption and rs671 (ALDH2)

	Non-drinking			Low			Intermediate			High		
	ALDH2 rs671			ALDH2 rs671			ALDH2 rs671			ALDH2 rs671		
	GG	GA+AA	GA+AA	GG	GA+AA	GA+AA	GG	GA+AA	GA+AA	GG	GA+AA	GA+AA
HAXA												
Age	54.7±7.7	54.4±7.9	52.1±7.8	52.1±7.8	52.5±8.3	53.3±8.2	53.3±8.2	52.6±8.2	52.7±7.9	52.0±7.5		
Systolic blood pressure	121.7±15.2	121.3±14.5	120.9±14.6	121.0±13.9	121.0±13.9	124.9±14.4	123.9±13.3	123.9±13.3	124.9±15.8	124.9±15.8		
Diastolic blood pressure	74.8±9.6	74.8±9.5	74.8±9.7	75.2±9.3	75.2±9.3	78.0±9.7	77.2±9.2	77.2±9.2	78.2±10.9	78.2±10.9		
Fasting glucose	93.7±18.9	93.8±18.8	93.2±17.6	93.7±17.3	93.7±17.3	98.1±20.8	94.2±15.6	94.2±15.6	94.9±18.2	94.9±18.2		
HDL-cholesterol	54.3±12.8	52.9±12.6	55.7±13.5	51.9±12.8	51.9±12.8	53.0±13.3	50.9±11.9	50.9±11.9	53.8±13.8	53.8±13.8		
Triglycerides	116.6±72.9	121.0±76.8	112.9±74.3	121.4±75.7	121.4±75.7	141.5±102.3	130.1±81.1	130.1±81.1	147.2±108.7	147.2±108.7		
CAVAS												
Age	60.4±8.9	61.1±8.7	58.9±9.0	59.9±8.0	59.9±8.0	59.5±8.9	59.8±10.4	59.8±10.4	60.8±8.7	60.8±8.7		
Systolic blood pressure	126.6±17.7	126.7±18.3	127.6±17.9	127.3±17.4	127.3±17.4	128.9±17.6	127.4±17.5	127.4±17.5	137.0±19.3	137.0±19.3		
Diastolic blood pressure	79.6±11.1	79.4±11.2	80.5±10.8	81.2±10.1	81.2±10.1	82.4±11.6	82.7±12.5	82.7±12.5	87.2±9.9	87.2±9.9		
Fasting glucose	98.5±23.7	98.8±23.5	102.3±24.8	99.3±21.6	99.3±21.6	102.6±20.7	96.4±15.5	96.4±15.5	95.1±8.2	95.1±8.2		
HDL-cholesterol	45.8±10.8	45.6±10.8	46.7±11.5	42.4±10.5	42.4±10.5	45.8±11.5	47.6±12.0	47.6±12.0	57.6±20.5	57.6±20.5		
Triglycerides	149.6±89.4	143.1±79.1	144.9±88.7	160.3±122.9	160.3±122.9	169.8±121.0	146.9±77.3	146.9±77.3	141.7±148.9	141.7±148.9		
KARE												
Age	53.1±8.7	52.5±8.6	50.7±8.2	49.2±7.8	49.2±7.8	50.0±7.9	50.0±8.5	50.0±8.5	50.2±8.8	50.2±8.8		
Systolic blood pressure	121.9±19.4	120.6±18.2	118.7±18.0	116.6±15.9	116.6±15.9	120.6±16.5	120.7±16.4	120.7±16.4	119.3±16.7	119.3±16.7		
Diastolic blood pressure	79.4±11.4	79.2±11.3	78.7±10.9	78.8±10.0	78.8±10.0	81.3±10.6	82.1±10.2	82.1±10.2	79.8±11.5	79.8±11.5		
Fasting glucose	90.7±19.5	90.6±19.3	90.4±18.6	88.6±13.4	88.6±13.4	94.7±25.3	91.5±19.7	91.5±19.7	94.5±27.7	94.5±27.7		
HDL-cholesterol	49.4±11.1	48.5±11.3	51.1±12.1	47.1±10.1	47.1±10.1	49.3±11.4	46.7±10.2	46.7±10.2	48.8±8.8	48.8±8.8		
Triglycerides	141.3±93.8	143.5±99.1	140.1±109.4	130.2±87.7	130.2±87.7	172.8±124.0	163.2±125.0	163.2±125.0	173.8±133.7	173.8±133.7		

HEXA, Health examines cohort; CAVAS, Cardiovascular disease association study; KARE, Korean association resource

Table 6. Distribution for type 2 diabetes and hypertension according to alcohol consumption and rs671 (ALDH2)

	Non-drinking	Low	Intermediate	High
Hypertension				
rs671 (ALDH2)				
GG	6,020 (30.7)	2,484 (26.2)	3,264 (34.8)	2,009 (40.9)
GA+AA	3,908 (28.4)	632 (24.3)	471 (30.0)	104 (29.5)
Type 2 diabetes				
rs671 (ALDH2)				
GG	1,717 (9.0)	652 (7.0)	961 (10.5)	626 (12.9)
GA+AA	1,147 (8.5)	158 (6.2)	98 (6.4)	18 (5.2)