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Greater Risk of Ascitic Cirrhosis in Females in Relation to Alcohol Consumption

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Tuyns A J (International Agency for Research on Cancer, 150 cours Albert Thomas, F-69372 Lyon Cedex 08, France) and Pequignot G. Greater risk of ascitic cirrhosis in females in relation to alcohol consumption. *International Journal of Epidemiology* 1984, **13**: 53–57.

The risk of ascitic cirrhosis increases with average daily consumption of alcoholic beverages, both in males and in females. For the latter, however, the curve is much steeper, indicating a greater risk for the female liver, with the disease occurring earlier in life. Health implications are discussed.

In a previous paper,[1] we described how the risk of ascitic cirrhosis was related to average daily intake of alcohol in the French department of Ille et Vilaine and we suggested that the dose-response relationship be confirmed by further studies in other populations.

This paper describes a study carried out in the population of Calvados, another French department on the West Coast of France, using more data and thus enabling comparisons between males and females.

DESIGN OF STUDY, MATERIAL AND METHODS

The design of the study was basically the same as the one performed in Ille et Vilaine.[2] All 417 cases of ascitic cirrhosis hospitalized in the various hospitals in Calvados between 1975 and 1979 were interviewed about their dietary, drinking and smoking habits, using a questionnaire identical to the one used before. In addition to being asked about their drinking habits just before the disease was diagnosed, they were also asked about their consumption before that period: the changes in type of beverage and amount consumed which may have occurred during their lives were also taken into account.

The 1976 controls represented a 5.4‰ sample of the total adult population of the department; this sample was selected by a two-stage procedure as described previously.[3] The response rate was 76.3%.

Based on the drinking history of the individual, average daily intake over the adult life-time was calculated for each beverage (beer, cider, wine, aperitifs and digestives (strong liquors). The equivalent in grammes of pure alcohol was derived on the following basis (for 100 cc.):

beer	4 g.
cider	3 g.
wine	8 g.
aperitifs	14 g.
digestives	36 g.

Total daily intake was computed and the analysis made for nine consumption classes: 0–19 g, 20–39 g. and so on. The first class was taken as a reference to calculate relative risks in the other consumption classes.

RESULTS

Age and sex distribution of patients with ascitic cirrhosis and controls

This distribution is shown in Table 1. More than half of the male cases (58%) occurred between the ages of

TABLE 1 *Ascitic cirrhoses and controls, by sex and age.*

	Ascitic cirrhoses				Population controls	
	Males		Females		Males	Females
Age	No	%	No	%	No	No
< 25	1	0.4	—	—	82	92
25–34	7	2.6	4	2.7	174	211
35–44	26	9.7	31	20.8	159	184
45–54	65	24.3	42	28.2	168	203
55–64	74	27.6	38	25.5	146	139
65–74	81	30.2	27	18.1	107	133
75+	14	5.2	7	4.7	87	90
Total	268	100.0	149	100.0	923	1053

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TABLE 2 *Ascitic cirrhoses and controls: distribution into daily alcohol consumption classes, in grammes of pure ethanol.*

Daily consumption in grammes	Ascitic cirrhoses				Population controls			
	Males		Females		Males		Females	
	No	%	No	%	No	%	No	%
0–19	5	1.9	32	21.5	222	24.1	815	77.4
20–39	21	7.8	32	21.5	228	24.7	180	17.1
40–59	30	11.2	36	24.2	225	24.4	40	3.8
60–79	41	15.3	19	12.8	112	12.1	12	1.1
80–99	50	18.7	8	5.4	64	6.9	6	0.6
100–119	45	16.8	13	8.7	33	3.6	—	—
120–139	26	9.7	6	4.0	23	2.5	—	—
140–159	14	5.2	—	—	7	0.8	—	—
160+	36	13.4	3	2.0	9	1.0	—	—
Total	268	100.0	149	100.0	923	100.0	1053	100.0

55 and 75, while in females 54% appeared between 45 and 65.

The distribution of controls reflects the age structure of the total population from which they were drawn.

Distribution of cases and controls by daily alcohol consumption classes (Table 2)

As compared with controls, the distribution of patients with cirrhosis is shifted towards higher consumption classes, for both males and females.

For patients as for controls, consumption was much greater in males than in females.

These two main features appear in Figure 1; the distribution of female cirrhotics is close to that of male population controls.

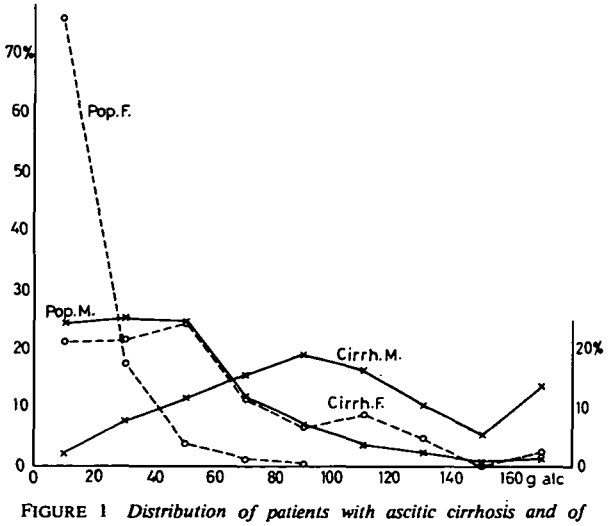

FIGURE 1 *Distribution of patients with ascitic cirrhosis and of population controls by daily consumption of alcohol.*

Relative risk of ascitic cirrhosis by daily alcohol consumption

After direct adjustment for age, required by the different age structure of controls and cases, expected numbers were obtained which are shown in Table 3 together with observed numbers.

Relative risks derived from these numbers in each consumption class also appear in the table.

These risks have been represented in Figure 2, all classes above 80 g a day being regrouped to make the two series for males and females comparable. The regression curves have also been shown; their expression is:

—for males: $\log RR = c_a \cdot 0.01164 + 0.14549$
—for females: $\log RR = c_a \cdot 0.02189 - 0.04724$

RR is the relative risk of ascitic cirrhosis and c_a the average daily consumption of alcoholic beverages expressed in grammes of pure ethanol.

The slope is steeper for females than for males. The fit is good for males; it is not so good for females.

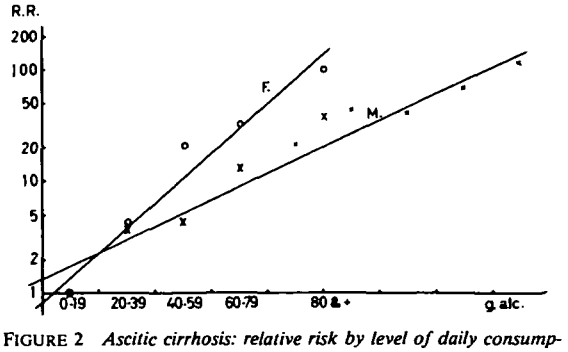

FIGURE 2 *Ascitic cirrhosis: relative risk by level of daily consumption of alcohol.*

TABLE 3 *Ascitic cirrhoses and controls, adjusted for age: relative risks in each consumption class.*

Daily consumption in grammes	Males			Females		
	Obs	Exp	RR	Obs	Exp	RR
0–19	5	54.02	1.00	32	112.71	1.00
20–39	21	63.08	3.60	32	27.28	4.13
40–59	30	69.75	4.65	36	5.87	21.60
60–79	41	32.88	13.47	19	2.08	32.17
80–99	50	25.01	21.60			
80+	(171)	(48.24)	(38.30)	30	1.06	99.68
100–119	45	10.90	44.60			
120–139	26	6.77	41.49			
140–159	14	2.26	66.93			
160+	36	3.30	117.86			
Total	268	267.97		149	149.00	

TABLE 4 *Attributable percentages and numbers of cases of ascitic cirrhosis.*

Daily alcohol consumption in grammes	Males				Females			
	Obs	RR	Attr %	Attr no of cases	Obs	RR	Attr %	Attr no of cases
0–19	5	1.00	—	—	32	1.00	—	—
20–39	21	3.60	72.2	15.2	32	4.13	75.8	24.3
40–59	30	4.65	78.5	23.5	36	21.60	95.4	34.3
60–79	41	13.47	92.6	38.0	19	32.17	96.9	18.4
80+	171	38.30	97.4	166.5	30	99.68	99.0	29.7
Total	268		(90.7)	243.2	149		(71.6)	106.7

Attributable percentage and number of cases

These are presented in Table 4. The total number of cases attributable to alcohol consumption in males is 243.2, ie 90.7% of the total; in females, the number is 106.7, ie 71.6% of the total. Thus, the number of ascitic cirrhoses not attributable to alcohol consumption is 24.8 in males and 42.3 in females.

DISCUSSION

Only cirrhotic cases with ascitis have been included in the study as such cases require hospitalization, compared with less severe cases of cirrhosis which are often treated on an ambulatory basis by general practitioners. The latter are difficult to trace and their definition unsafe as diagnosis is not easy at the early stage of the disease; patients may further report at various degrees of development of their illness; many do not consult till they reach the stage of ascitis.

No distinction was made between cases of ascitis clinically considered to be related to alcohol and other cases. There is no satisfactory clinical or pathological definition of alcoholic cirrhosis. Such lesions as steatosis or 'alcoholic' hepatitis which often accompany cirrhosis are frequently related to excessive drinking but they cannot be attributed exclusively to alcohol.[4] On the other hand, heavy alcohol consumers may present lesions of chronic hepatitis which are not classically considered to be caused by alcohol.[4]

In fact, when a clinician or a pathologist diagnoses an 'alcoholic' cirrhosis, he takes into account what the patient declares and he appreciates the 'excessive' drinking in relation to standards which may vary considerably. No one would dare incriminate alcohol if a patient consumed some 40–50 g per day since this would not be considered as excessive by French standards. This corresponds to no more than half a litre of wine or a litre of beer; yet, at this level the relative risk is already 4.7, as can be seen in Table 3.

The increase of risk with level of consumption is a phenomenon which makes sense biologically; it leaves open the question of the 'safe threshold' which, on the basis of our data, could be set at 20 g per day. There is no indication, however, that the continuous line observed at higher doses should start at that level and not below: the only reason why we set the limit at 20 g is that we needed a sufficient number of cases in our lower consumption class to calculate relative risks in the others. In other words, there is a threshold below which the calculation of risks is very hazardous and the increase of risk, if any, is minimal. There is a threshold

below which it is difficult if not impossible to conclude safely that there is already an increase or not; whether this corresponds or not to a biological threshold is a matter of individual conjecture.

The shape of the relative risk curve for males is identical to that observed previously in Ille et Vilaine.[1] In our first study, however, the level of increase was such in females that we decided not to incorporate them in our first analysis but to wait until more data were available from Calvados. It is now clear that the risk of ascitic cirrhosis increased with daily alcohol intake much faster in females than in males.

One may argue that alcohol consumption by women is less socially acceptable than it is for males; hence the consumption acknowledged by the female population used as a control group would be underestimated to fit what is socially acceptable. The risk values would consequently be overestimated. One may object to this reasoning since, if some distortion of this kind affects female controls, it should also affect the female cases of cirrhoses.

One may also argue that bodyweight has not been taken into account in our estimates and that it may bring about a more rapid increase of risk in females whose weight may be 10–30% lower than that of males. The argument is valid but the level of increase is far greater than one would expect if a correction of 10–30% was made.

It is common clinical experience that women develop liver disease after a shorter time and less exposure to alcohol than men.[5,6]

Our findings confirm and clarify these statements. The earlier occurrence of ascitic cirrhosis in females is illustrated by Figure 3. As for the influence of the level of exposure, Figure 2 shows that even small doses of alcohol of the order of 40 g a day, which moderately increase the risk in males (relatively speaking) entail a considerable increase in females. This indicates a greater susceptibility of the female liver to the action of alcohol.

Several comments are relevant on Table 4. If the limit of 80 g of alcohol was set as a 'safe' limit, as has been suggested for a long time in the past, 171 out of 268 cases would have been avoided among males (64%), but no more than 20% (30/149) in females; even by setting the limit at 40 g a day, no more than 57% of female cases would be avoided compared with 90% in males.

Another remark concerns the cases of ascitic cirrhosis that are *not* attributable to alcohol. Assuming that there would be no effect of alcohol below a daily intake of 20 g, which is the maximum for our reference consumption class, there would be 24.8 such cases in

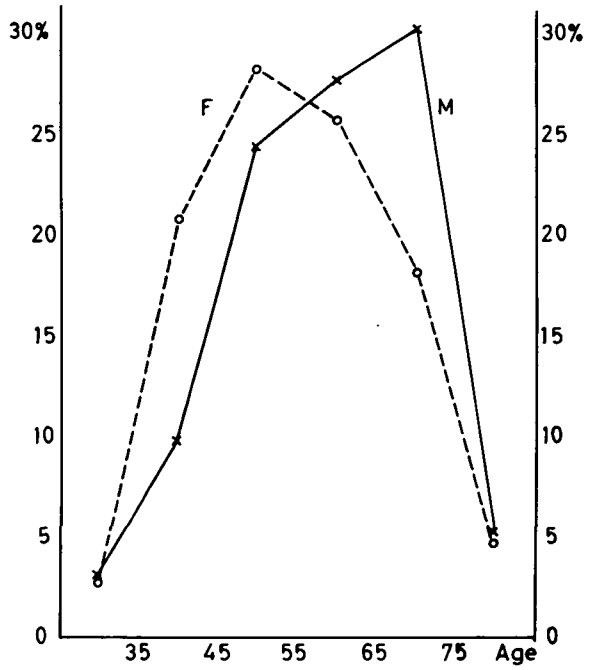

FIGURE 3 *Ascitic cirrhosis: age distribution.*

males and 42.3 in females. These would be cases related to other causes such as viral hepatitis or intoxication by agents other than alcohol. The greater number in females again may be the expression of a greater susceptibility of the female liver to these other causes as well. Considering the shape of the risk curves in males and females respectively (Figure 2) it is not unlikely, however, that even below the level of 20 g a day, alcohol might have a deleterious effect on the liver.

The practical implications of these findings are obvious. In present day society where women tend to increasingly share the work responsibilities and life styles of men, they tend to drink more alcohol. They participate more and more in social activities, they have better and easier access to alcoholic beverages than in the past and they are also influenced by clever advertisements directed at women. The role of these factors in contemporary women's life has been reviewed by Shaw.[7] The consequences in terms of cirrhosis are likely to be dramatic.

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