Ovarian cancer and ABO blood groups

Jane Henderson, Valerie Seagroatt, Michael Goldacre

Abstract

Objective—To determine whether the distribution of ABO blood groups in women with ovarian cancer differs from that in the general population in a large, defined English region.

Design—Analysis of record abstracts of hospital care held in the Oxford record linkage study supplemented with data from the Oxford cancer registry.

Setting—Oxford Regional Health Authority area.

Subjects—A total of 1261 women who had ovarian cancer between 1968 and 1986 with ABO blood groups recorded on the Oxford Record Linkage Study and cross checked against the cancer registry comprised the study group.

Measurements and main results—The relative incidence of A:O and B:O blood groups in women with ovarian cancer were compared with the general population in the same region. Ovarian cancer was more common in women of blood group A than in others, with a relative incidence of 1.17. In particular, adenocarcinomas were the most common type of tumour and were associated with blood group A. The association was more striking in married women than in single women probably reflecting differences associated with parity.

Conclusion—The association between ABO blood groups and ovarian cancer found in this English population is similar in size to that reported from several other populations. Childbearing is known to reduce the risk of ovarian cancer and our findings suggest that the blood group association may be most apparent in married, parous (that is, relatively low risk) women.

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About 4000 women die each year from ovarian cancer in England.1 It is the commonest cause of death from cancer of the female genital tract in England and its prognosis is generally poor.2 3 Death rates increased in England during the first half of this century but have levelled off in recent decades.4 5 It is commoner in western Europe and north America than in Japan, China, India, and south America.6 The aetiology of ovarian cancer is largely unknown and its study is complicated by the many different histological types of tumour. There is a protective effect of parity and of the use of oral contraceptives.7 8

For some cases, it has long been suspected that there is a genetic influence. Clustering within families occurs. McGowan, for example, found that women with ovarian cancer were more likely than controls to have relatives with cancer of the female reproductive organs.9 There is also evidence that breast cancer and ovarian cancer may occur together in families more often than expected by chance.10 Several studies from elsewhere have suggested an association between ovarian cancer and blood group A as a genetic marker.11-14 We are not, however, aware of large scale, population based investigations of this association in an English population. The Oxford Record Linkage Study is probably one of the largest datasets available which includes data on ABO blood groups and clinical disease and we therefore used its data to examine this relationship in Oxford.

Method

PATIENTS AND RECORDS
The Oxford Record Linkage Study (ORLS) is a collection of brief statistical abstracts of hospital records in a defined population in the Oxford region. When the patient's blood group is recorded in the case notes during an inpatient stay, the data have been routinely coded on the ORLS abstract. In the present study, if blood group was not recorded on the record of ovarian cancer, where available it was taken from other records relating to the woman. The study included women with a primary diagnosis of malignant neoplasm of the ovary (International Classification of Diseases' codes 183.0 in the 8th and 9th revisions) admitted to National Health Service hospitals in the two districts of the Oxford region covered by data collection between 1968 and 1974 and the six districts covered by data collection between 1975 and 1986. The diagnosis of ovarian cancer was cross checked with the Oxford region's cancer registry and information on the histological type of the tumour was obtained from that source.

Data on blood groups for controls were available from three sources. These were: all patients in the ORLS whose blood group had been recorded between 1968 and 1978; all patients in the ORLS with a blood group recorded between 1979 and 1984; and blood donors in the Oxford region in 1988. ABO blood group distribution in each source were very similar, and we used the inpatient data for 1979–84 as the control data in the statistical analyses which follow.

STATISTICAL METHODS
The blood group distribution of the cases and the control population were compared by the method
The blood group distributions and relative incidences for groups A and B by histological tumour type are shown in table I. The relative incidences of A and B were greater than one in the patients with ovarian cancer. That for blood group A differed significantly from one (χ²=7.0; df=1; p<0.01). The confidence intervals for the relative incidences for B were based on many fewer cases and were much wider than those for blood group A.

The relative incidence of blood group A in patients with adenosarcoma was 1:15 (95% confidence interval 1:0, 1:3). Although special ovarian tumours and other epithelial tumours had lower relative incidences for A and B, numbers were small, the confidence intervals were wide, and these differences were not significant. Overall, the differences found in the relative incidences for both A and B, comparing different historical types, were not significant (χ² for A:O=5.4; B:O=2.7; 4 degrees of freedom).

In the general population, even within the United Kingdom, ABO blood group distributions are strikingly associated with place of birth. In the ORLS population the A:O ratio was highest in people born in south and central England (table II). We therefore examined the blood group association for those born in south or central England separately. The place of birth was recorded for 1117 of the 1261 patients with ovarian cancer (99%). Of the 1117, 819 women were born in south and central England. Of these, 379 were blood group O and 440 were blood group A. The relative incidence of A:O in patients with ovarian cancer born in south and central England was 1:16 (95% confidence interval 1:0, 1:3).

The relative incidences of blood group A in women with ovarian cancer subdivided by marital status, adjusted for age, are shown in table III. The relative incidence for single women was lower than that for married women, and that for divorced and widowed women was intermediate between the single and married women. These differences were statistically significant. Restricting our analysis to those born in south or central England, single women still had the lowest relative incidence but the numbers were smaller, the variation was reduced, and the differences no longer significant. We assumed that marital status was a proxy for parity in respect of the blood group association. We therefore sought data on parity from the ORLS files. Parity has not been regularly recorded on gynaecological records in the ORLS and was available for only 349 (29%) of the cases. Since information on parity was not available for

<table>
<thead>
<tr>
<th>Histological type</th>
<th>Total</th>
<th>No (%) with stated group</th>
<th>Relative incidence A:O</th>
<th>95% confidence interval</th>
<th>Relative incidence B:O</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ovarian cancers</td>
<td>1261</td>
<td>518 (41.1%) 587 (46.6%) 114 (9.0%)</td>
<td>42 (3.3%)</td>
<td>1:17 (1:0, 1:3)</td>
<td>1:10 (0:9, 1:4)</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>1011</td>
<td>420 (41.5%) 465 (46.0%) 93 (9.2%)</td>
<td>33 (3.3%)</td>
<td>1:15 (1:0, 1:3)</td>
<td>1:10 (0:9, 1:4)</td>
<td></td>
</tr>
<tr>
<td>Anaplastic tumours</td>
<td>73</td>
<td>32 (43.8%) 33 (44.7%) 8 (11.0%)</td>
<td>0 (0.0%)</td>
<td>1:07 (0:6, 1:8)</td>
<td>1:25 (0:6, 2:7)</td>
<td></td>
</tr>
<tr>
<td>Special ovarian tumours</td>
<td>47</td>
<td>21 (47.8%) 20 (44.7) 2 (4.4%)</td>
<td>0.99 (0:5, 1:8)</td>
<td>0:47 (0:1, 2:1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other epithelial tumours</td>
<td>47</td>
<td>23 (47.8%) 23 (47.8) 1 (2.2%)</td>
<td>0.85 (0:3, 2:1)</td>
<td>0:49 (0:1, 3:7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td>107</td>
<td>34 (31.8%) 60 (56.1) 13 (9.3%)</td>
<td>1:83 (1:2, 2:8)</td>
<td>1:47 (0:7, 3:0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Controls were the ORLS patients admitted during 1979-84.

*Relative incidence differs from one at 5% level.

Table II Blood group distribution of general hospitalised population (ORLS 1979-84) by place of birth

<table>
<thead>
<tr>
<th>No (%) with stated group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>A</td>
</tr>
<tr>
<td>South and Central England (%)</td>
<td>29703</td>
</tr>
<tr>
<td>North England and Scotland (%)</td>
<td>4610</td>
</tr>
<tr>
<td>Wales (%)</td>
<td>794</td>
</tr>
<tr>
<td>Ireland (North and South) (%)</td>
<td>1922</td>
</tr>
<tr>
<td>Other countries (%)</td>
<td>2860</td>
</tr>
<tr>
<td>Not known (%)</td>
<td>9800</td>
</tr>
</tbody>
</table>

Jane Henderson, Valerie Seagroat, Michael Goldacre Described by Mourant, citing Woolf. The ratio of the frequency of blood group A to O in the cases was calculated first, followed by the ratio of blood group A to O in the controls. The ratio of the A:O ratio for the cases to that for the control population was then calculated and, following Mourant, this was termed the relative incidence of A. In effect, this provides a measure of relative incidence of A to O blood groups in the cases after adjusting for the levels of A and O in the control population. If the cases and controls had the same blood group distributions in respect of A and O, then the relative incidence would be one. A χ² statistic for the significance of the difference of the estimated relative incidence from one and its approximate confidence interval were calculated. Similar calculations were undertaken to compare the relative incidences of blood group B to O in cases and controls.

The heterogeneity of relative incidences estimated in subgroups of the cases (for example, comparing histological types, marital status groups, and parity groups) was assessed by χ² statistic. Relative incidences for subgroups of the cases were combined by taking their weighted geometric mean with weights taken as the reciprocal of the variances of the individual incidences.

Results

Data on 1261 women with ovarian cancer and recorded ABO blood groups were available for analysis. As expected, most tumours were adenocarcinomas. Using the cancer registry's nomenclature, there were 1011 adenocarcinomas (80.2% of the total), 73 tumours recorded as anaplastic (15.8%), 47 "special ovarian" tumours (3.7%) which were mainly granulosa cell tumours, 23 "other epithelial" tumours (1.8%) which included sarcomas, and the histology was unspecified in 107 patients (8.5%).
the controls, we used the blood group data on single women in the ORLS files as controls for
nulliparous cases; and we used the blood group data on married women as controls for parous
cases. As expected, nulliparous women had the lowest relative incidence but these differences
were not statistically significant (table III). We
analysed the data on blood group, marital status,
and parity again confining the analysis to women
born in south and central England with the same
result but a larger confidence interval.

Discussion
Mourant combined data on a total of 3175 cases
from 24 studies in different populations world-
wide to obtain a relative incidence for blood group
A:O of 1:23.15 Bjorkholm found a relative inci-
dence for blood group A:O of 1:19 in a study of
1930 women from a single centre in Sweden
(where the prevalence of blood group O in the
general population is lower than that in
England).13 Our relative incidence for A:O in
women with ovarian cancer in a fairly homo-

The 1991 report of International Agency for Research on Cancer also makes a virtue of
what is often a nightmare—excessively fine
subdivisions. An example is the study of ovar-
ian cancer risk by blood group, which is not
meaningful by itself, but only in combination
with other factors. This division and subdivi-
sion (some 100 in this case) is a red herring,
but one that has become extremely popular
in recent years. It is surprising that the
1991 report of IARC should have carried
forward this practice when it is only scientifi-
cally meaningful in well-controlled studies of
cohorts or case-control series of cases and
controls.

We would like to thank Jennie Fairweather for her
computing assistance and Liza Brandon for secretarial
help. The Unit of Health Care Epidemiology is part of
the Department of Public Health and Primary Care,
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Department of Health; the Oxford Record Linkage
Study is funded by Oxford Regional Health Authority.

Table III  Association
between blood group A, marital state, and parity
adjusted for age

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total women</th>
<th>Blood group A</th>
<th>Relative incidence</th>
<th>95% confidence interval</th>
<th>$\chi^2$ for comparison with controls (df=1)</th>
<th>$\chi^2$ for differences between marital state/parity groups (df=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital state:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>140</td>
<td>70</td>
<td>54</td>
<td>0:81</td>
<td>0:6-1:2</td>
<td>1:3</td>
</tr>
<tr>
<td>Married</td>
<td>771</td>
<td>296</td>
<td>376</td>
<td>1:27</td>
<td>1:1-1:5</td>
<td>0:0</td>
</tr>
<tr>
<td>Widowed</td>
<td>218</td>
<td>98</td>
<td>93</td>
<td>1:01</td>
<td>0:7-1:4</td>
<td>0:0</td>
</tr>
<tr>
<td>Divorced</td>
<td>77</td>
<td>32</td>
<td>35</td>
<td>1:13</td>
<td>0:7-1:9</td>
<td>0:2</td>
</tr>
<tr>
<td>Weighted average</td>
<td>1206</td>
<td>496</td>
<td>557</td>
<td>1:18</td>
<td>1:0-1:3</td>
<td>5:7</td>
</tr>
<tr>
<td>Parity:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>84</td>
<td>37</td>
<td>33</td>
<td>0:98</td>
<td>0:6-1:6</td>
<td>0:1</td>
</tr>
<tr>
<td>1</td>
<td>83</td>
<td>31</td>
<td>44</td>
<td>1:41</td>
<td>0:9-2:3</td>
<td>2:1</td>
</tr>
<tr>
<td>2</td>
<td>101</td>
<td>43</td>
<td>43</td>
<td>1:01</td>
<td>0:7-1:6</td>
<td>0:0</td>
</tr>
<tr>
<td>3+</td>
<td>81</td>
<td>34</td>
<td>40</td>
<td>1:16</td>
<td>0:7-1:9</td>
<td>0:3</td>
</tr>
<tr>
<td>Weighted average</td>
<td>349</td>
<td>145</td>
<td>160</td>
<td>1:12</td>
<td>0:9-1:4</td>
<td>1:0</td>
</tr>
</tbody>
</table>

*Significant at the 5% level

suggest that the association may be most evident in
women with a comparatively low risk of
developing ovarian cancer, that is, married parous
women. Investigators studying other, more discrim-
inating genetic markers, such as HLA anti-
gens, may find it useful to subdivide patient
populations by levels of known risk, such as parity,
in assessing the genetic contribution to the disease.

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