

# Blood Elements Levels and Cancer Risk in BRCA1 Mutation Carriers: A Prospective Study

Matuszczak M.<sup>1</sup>; Kiljańczyk A.<sup>1</sup>; Marciniak W.<sup>2</sup>; Derkacz R.<sup>2</sup>; Stempa K.<sup>1</sup>; Baszuk P.<sup>1,2</sup>; Bryśkiewicz M.<sup>1,2</sup>; Lubiński K.<sup>1</sup>; Pietrzak S.<sup>1</sup>; Huzarski T.<sup>1,2,4</sup>; Gronwald J.<sup>1,2</sup>; Cybulski C.<sup>1,2</sup>; Dębniak T.<sup>1</sup>; Lener M.<sup>1</sup>; Jakubowska A.<sup>1</sup>; Szwiec M.<sup>3</sup>; Stawicka-Niełacna M.<sup>4</sup>; Godlewski D.<sup>5</sup>; Prusaczyk A.<sup>6</sup>; Jasiewicz A.<sup>7</sup>; Kluz T.<sup>8</sup>; Tomiczek-Szwiec J.<sup>9</sup>; Kilar-Kobierzycka E.<sup>10</sup>; Siołek M.<sup>11</sup>; Wiśniowski R.<sup>12</sup>; Posmyk R.<sup>13</sup>; Tretyn-Jarkiewicz J.<sup>14</sup>; Scott R.<sup>15</sup>; Narod S.A.<sup>16</sup>; Lubiński J.<sup>1,2</sup>

<sup>1</sup> Department of Genetics and Pathology, International Hereditary Cancer Center, Pomeranian Medical University, ul. Unii Lubelskiej 1, 71-252, Szczecin, Poland,

<sup>2</sup> Read-Gene, Grzeczna, ul. Alabastrowa 8, 72-003, Dobra (Szczecińska), Poland,

<sup>3</sup> Department of Clinical Genetics and Pathology, University of Zielona Góra, ul. Zyty 28, 65-046 Zielona Góra,

<sup>4</sup> Department of Surgery and Oncology, University of Zielona Góra, Zyty 28, 65-046 Zielona Góra, Poland,

<sup>5</sup> OPEN, Kazimierza Wielkiego 24 St, 61-863, Poznań, Poland,

<sup>6</sup> Medical and Diagnostic Center, Siedlce, Poland,

<sup>7</sup> Genetic Counseling Center, Subcarpathian Oncological Hospital, 18 Bielawskiego St, 36-200, Brzozów, Poland,

<sup>8</sup> Department of Gynecology, Gynecology Oncology and Obstetrics, Institute of Medical Sciences, Medical College of Rzeszow University, Rejtana 16c, 35-959 Rzeszow, Poland,

<sup>9</sup> Department of Histology, Department of Biology and Genetics, Faculty of Medicine, University of Opole, Opole, Poland,

<sup>10</sup> Department of Oncology, District Specialist Hospital, Leśna 27-29 St, 58-100, Świdnica, Poland,

<sup>11</sup> Holycross Cancer Center, Artwińskiego 3 St, 25-734, Kielce, Poland, Poland,

<sup>12</sup> Regional Oncology Hospital, Wyzwolenia 18 St, 43-300, Bielsko Biała, Poland,

<sup>13</sup> Department of Clinical Genetics, Podlaskie Medical Center, Białystok, Poland,

<sup>14</sup> Non-Public Health Care Centre, Cancer Genetics Laboratory, 87-100 Toruń, Poland,

<sup>15</sup> Medical Genetics, Hunter Medical Research Institute; Priority Research Centre for Cancer Research, Innovation and Translation, School of Biomedical Sciences and Pharmacy, Faculty of Health and Medicine, University of Newcastle; Pathology North, John Hunter Hospital, King and Auckland Streets, Newcastle NSW 2300 Australia,

<sup>16</sup> Women's College Research Institute, Women's College Hospital, University of Toronto, Toronto, ON M5G 1N8, Canada

## Abstract:

Women with BRCA1 mutations face a significantly elevated risk of breast and ovarian cancers, with lifetime risks of approximately 70% and 40%, respectively. Given this high cancer risk, our study aimed to investigate whether modifiable factors, particularly blood elements levels, could influence cancer risk in this population. We prospectively observed 1,204 initially healthy BRCA1 mutation carriers, most of whom were younger than 50 years (mean age 39). During the 7.5-year follow-up, 206 cancer cases were diagnosed, including 143 breast cancers, 38 ovarian cancers, and 25 other malignancies.

Using ICP-MS, we measured the concentrations of 23 trace elements (Ag, As, Br, Ca, Cd, Co, Cs, Cu, Fe, Hg, I, Li, Mg, Mn, Mo, Ni, P, Pb, Se, Sn, Sr, Ti, V, Zn) in the blood of all participants. The cohort was divided into tertiles based on these elements levels. Cox proportional hazards regression was applied to assess the relationship between elements levels and cancer risk.

Our analysis identified several significant findings. High silver levels were associated with a 6.5-fold increased risk of ovarian cancer, while low cobalt levels reduced ovarian cancer risk nearly threefold. Elevated iodine levels posed a significant danger, increasing ovarian cancer risk by 3.7 times. Similarly, high levels of lithium, molybdenum, vanadium, and zinc were linked to varying cancer risks. An additive protective effect was observed when optimizing multiple elements, with silver, cobalt, lithium, iodine, molybdenum, vanadium, and zinc levels showing an eightfold difference in ovarian cancer risk.

In breast cancer, optimal levels of iodine, phosphorus, and lead modestly reduced risk, and a combined effect of lead and molybdenum resulted in a nearly fourfold reduction. The zinc-to-copper ratio also demonstrated a 1.53-fold reduction in the risk of any cancer. Furthermore, lower levels of cadmium, copper, iodine, and lead were associated with improved overall survival, with lead having the strongest impact on all-cause mortality (a fourfold reduction in risk).

In conclusion, trace elements may serve as important markers of cancer risk in BRCA1 mutation carriers, and their optimization could offer a modest reduction in cancer risk. However, preventive surgeries and regular screenings remain the most effective risk-reduction strategies for this high-risk population. Understanding the interactions between trace elements could offer additional insights for risk management.