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Research

A small-scale test of whether alkalizing diets can reduce the risk of disease as predicted by the Warburg Hypothesis

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Diet and so-called dietary acid load have a significant effect on what have traditionally been called acid-base disorders and various disease states, including cancer. However, the effect has been poorly investigated, and standards of care in medical treatments for cancer patients generally do not consider monitoring acid-base disorders and resolving them using dietary interventions.

This paper begins by explaining the Warburg Hypothesis, focusing on dietary interventions thought to help maintain acid-base balance and reduce inflammation at the cellular level, as reflected in certain venous blood parameters. By integrating traditional and modern nutritional sciences for preventing and managing cancer, potential dietary interventions are identified that may help maintain nutritional status. In addition, data on the efficacy of these nutritional interventions are presented, where the effect of following an alkalizing diet for 1-3 months is measured through venous blood gas parameters. Of 30 volunteers, 10 followed the prescribed diet for an entire month and their venous blood gas parameters before and after the diet were compared. There appeared to be a significant impact of the diet on these parameters. Thus, we speculate that the prescribed alkalizing diet may be an effective practice to eliminate acid-base disorders and reduce its impact on cancer and other diseases. Further research should examine on a larger sample over a longer period of time, using additional parameters, whether such a diet could have an impact on the incidence or development of the cellular acid-base balance, levels of inflammation, and eventually various diseases, including cancer.

INTRODUCTION

In some traditions, it is believed that reducing acid load at cellular level via the diet may significantly lower the risk of inflammation and of developing various diseases, including cancers (Wu et al. 2019; Bahrami and Greiner 2021). However, the effect has been poorly investigated, and the related mechanisms and diet-based treatment strategies are unclear concerning what diet might actually be effective in achieving relevant improvements. Thus, modern medicine has not given attention to this issue and standards of care in medical treatment of cancer do not include relevant monitoring (Doyle et al. 2006; Bahrami, Tafrihi, and Mohamadzadeh 2022).

The link between cancer and cellular-level acidosis was first discovered by Dr. Otto Warburg (1883–1970), a German medical scientist and a Nobel Prize winner in Physiology and Medicine. Warburg's experimental studies showed that cancerous tumor cells utilize anaerobic cellular respiration processes that consume large amounts of glucose and produce lactic acid at a high rate that acidifies the cellular environment, a discovery that was later referred to as the Warburg effect (Otto 2016). Warburg's hypothesis postulates that the initiation of cancer and the growth of cancerous tumors are caused by the non-oxidative breakdown of glucose, so carcinogenicity is caused by the reduction in mitochondrial respiration (Zong, Rabinowitz, and White 2016; Bahrami and Tafrihi 2023b).

Warburg's experimental investigations showed that depriving a cell of 35% of oxygen just for 48 hours could make it cancerous (International Society for Children with Cancer 2015), suggesting that hypoxia (lack of oxygen) at the cellular level may be a major cause of cancer (Bode and Dong 2009). In hypoxic areas of the body, such as breast tissues in women and prostate tissues in men, chronic poor oxygenation increases the risk of mutations and gradual transformation of normal cells into cancer cells (Bahrami and Tafrihi 2023b; Bode and Dong 2009), which leads to

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anaerobic cellular respiration and lactic acidosis, according to the Warburg effect (Bahrami and Greiner 2021; Bahrami and Tafrihi 2023a). This situation results in inflammation in surrounding cells and other parts of the body (Choi et al. 2013), which leads to development of more invasive cancer cells and cancer metastasis (El-Kenawi et al. 2019; Dong, Krewson, and Yang 2017; Ibrahim-Hashim and Estrella 2019; Lee and Griffiths 2020).

Cancers may also be caused by other factors, such as significant exposure of body cells to carcinogenic substances, in which case the cells also use anaerobic cellular respiration and gradually become cancerous. However, since the main cause of cancer in this case is exposure to a carcinogen, and lack of oxygen is not the main cause, an increase in the rate of glucose uptake and preferential production of lactate according to the Warburg effect may occur even in the presence of sufficient oxygen (Bahrami and Tafrihi 2023b).

In addition to the associations between acidosis and cancer, a lower pH in the blood may also be linked to other diseases such as reduced bone density, osteoporosis, bone fracturing, and formation of kidney stones (Bahrami and Greiner 2021; Farshbaf-Khalili et al. 2022; Wang et al. 2022), for which the risk is more significant in older people, because they gradually lose some renal acid-base regulatory function, reducing the effectiveness of the buffering mechanisms in the body (Hietavala, Stout, et al. 2014). When our blood becomes more acidic, bone minerals neutralize this, which results in reduced bone density, increasing the risk of osteoporosis and bone fracturing (Bahrami and Greiner 2021). Hence, a frequent high intake of acid-forming foods such as animal proteins, including that from dairy products, may leach more calcium from the bones than is ingested, leading to higher risk of bone depletion and hip fractures (Lang 1996; Michaelsson et al. 2014).

Although Warburg's experiments successfully characterized metabolism in cancer cells in his laboratory, he did not do research in humans, and he did not study how to resolve the acidosis associated with cancer. Later, some natural health practitioners proposed an alkaline diet to reduce dietary acid load and eliminate acidosis for a better management of cancer and cancer-like conditions (Corriher 2009; Bridgeford 2015). The alkaline diet was originated from the research published by Robert Young in 2002 based on an analysis of over 40,000 live blood samples studying whether foods were acid-forming or alkaline-forming (Wang et al. 2022). However, his live blood analysis was not was not accepted as a standard laboratory practice, and, thus, the efficacy of alkaline diet has remained uncertain (Bahrami and Greiner 2021; U.S. Department of Health and Human Services 2001).

Potential renal acid load (PRAL) was introduced by Remer and Manz in 1995 to estimate dietary acid load based on a 'simple' formula that calculates capacity of acid or base production for various foods as a function of the protein, phosphorus, potassium, magnesium, and calcium content of foods (Remer and Manz 1995; Toba et al. 2019). However, there are numerous uncertainties in determining the actual dietary acid load using calculated PRAL values, as they are based on urine pH or a simple formula, but not on comprehensive analysis based on direct measurements of venous blood acidity (Bahrami and Greiner 2021; Storz and Ronco 2023; Parmenter, Dymock, et al. 2020). Furthermore, studies on the relationship between PRAL values of foods and cancer have been contradictory, as some found no association between cancer and PRAL scores (Safabakhsh et al. 2020), while others showed that a higher acid load according to PRAL values may lead to an increased risk of cancer (Keramati et al. 2022). Therefore, the reliability of calculated indicators of food acid and alkaline producing properties, such as PRAL, remained questionable and unproven.

Robert Young's values and PRAL values from Remer and Manz (Remer and Manz 1995) sometimes disagree. For instance, while they both classify beef and cow's milk as acidogenic (a positive dietary acid load), coffee, black tea, and beer are classified as foods with a negative dietary acid load (alkalizing) based on Remer and Manz PRAL values, but are acidogenic according to Young (Farshbaf-Khalili et al. 2022; Wang et al. 2022; Hietavala, Stout, et al. 2014).

Supporting Young are studies finding that alcohol intake is associated with a significant increase in osteoporotic and hip fracture risk (Kanis et al. 2005), consumption of green coffee supplements may reduce calcium in bones (Abbass and ELBaz 2018), and a high intake or regularly drinking coffee is associated with a higher hip fracture risk (Dai et al. 2018; Kiel et al. 1990), suggesting that alcohol and coffee may be acid-forming (Bahrami and Greiner 2021). In addition to the acidogenic effect of alcohol and coffee, alcoholic beverages contain ethanol, which is carcinogenic to humans (Pflaum et al. 2016), and coffee products contain acrylamide, which is classified as a human carcinogen by the International Agency for Research on Cancer (Mojska and Gielecińska 2013a; Tamanna and Mahmood 2015). It should be noted that the amount of acrylamide in instant coffee is twice higher compared to freshly roasted coffee (Mojska and Gielecińska 2013b).

Some researchers claim that dietary changes may lead to changes in the pH of saliva or urine, but not the blood pH, assuming it remains constant, though they provide no evidence for this (Collins 2022; Leech 2023). Others claim that certain foods contribute to a significant release of acids into the blood stream (Farshbaf-Khalili et al. 2022; Wang et al. 2022; Lewis 2023).

Based on the Warburg hypothesis, some researchers have suggested that an anti-inflammatory, alkalizing diet may help to maintain normal blood pH at the cellular level, and reduce inflammation, and thus the risk of cancer (Phillips et al. 2019a; Erra Díaz, Dantas, and Geffner 2018; Coussens and Werb 2002; Phillips et al. 2019b; Harvard Health Publishing 2021; Spritzler 2022). However, the Warburg effect is often confused with providing oral anti-acids or "alkaline-water", which has no or even a negative impact on the acid-base imbalance at cellular level throughout the body (Bahrami and Greiner 2021). This is because their alkalinity is immediately neutralized in contact with stomach acid, not reaching the tumors cells (Farshbaf-Khalili et al. 2022). This confusion can do harm, such as a case, in which, the use of baking soda for treating a cancer patient caused her death (Fox News 2017).

This type of incorrect application of the Warburg effect in cancer treatment is due to failure to consider blood carbon dioxide content and oxygen saturation as key factors controlling blood pH at the cellular level, as well as the important role of adequate oxygenation in maintaining aerobic cellular respiration (Bahrami and Greiner 2021; Farshbaf-Khalili et al. 2022). Particularly, in the hypoxic regions of the body, providing optimal alkalinity and sufficient oxygenation at the cellular level may result in a metabolic switch from anaerobic to aerobic, which may inhibit cancer progression, while retaining healthy cells (Bahrami and Greiner 2021).

Dietary interventions may be effective for reducing acid load at the cellular level. This involves the sufficient consumption of foods that are alkalizing at cellular level – but not necessarily alkaline when consumed. Table 1 presents a relevant food chart that can be used as a guide for preparing balanced meals (Bahrami and Greiner 2021; Bahrami, Tafrihi, and Mohamadzadeh 2022). The table suggests that alkalizing foods are plant foods and animal foods often have an acidifying effect (Bahrami and Greiner 2021). Interestingly in this context, research has also found that a high cholesterol diet benefited breast cancer cells (Esteves 2021).

Epidemiological and laboratory investigations suggest that improving health requires consuming more natural foods and limiting the consumption of processed and especially ultra-processed foods (Bahrami, Tafrihi, and Mohamadzadeh 2022). Food processing aimed at extending shelf life for commercial purposes may often reduce the nutritional value of the food (due to the loss of dietary fiber, B vitamins, phytochemicals, and some minerals), as well as expose foods to excessive temperatures that destroys enzymes, good bacteria and heat-sensitive vitamins (Better Health Channel 2022; O.'Connor and Steckelberg 2023; Dadan et al. 2021). Also, in foods containing amino acids (such as potatoes, beans, seeds and grains), frying, roasting or baking at very high temperatures leads to the production of acrylamide, which is a carcinogen (Mojska and Gielecińska 2013a; Tamanna and Mahmood 2015). Moreover, processed and ultra-processed foods often contain added sugars, and/or unhealthy oils and fats, which are acid-forming additives, and therefore, processed foods, including even canned fruits, industrial juices and vegetarian canned soups may be acidogenic (Bahrami, Tafrihi, and Mohamadzadeh 2022; O.'Connor and Steckelberg 2023; Dadan et al. 2021).

Another concern regarding today's food chain is the long-term storage and preservation methods. Among the existing methods of food preservation, chilling and freezing are more common as they can reduce or prevent growth of microorganisms responsible for food decomposition without killing them. But storage in the refrigerator or freezing is not suitable for preserving all biological cells, and in some foods, it may cause irreversible physical and chemical changes, such as freezing cucumbers or storing raw potatoes and onions in the refrigerator or a freezer, which may destroy the structure of these foods (Dadan et al. 2021).

In the large scale of the food chain, the overall costs associated with cooling for storage are high and freezing may not always be cost-effective, hence, other industrial methods are also utilized in the food industry, such as salt preservation, though a high intake of salted foods may be associated with an increased risk of stomach cancer (Bahrami and Tafrihi 2023b). Another is food irradiation, which may form volatile toxic chemicals or create unique radiolytic products in foods, substances that can cause gene mutations and cancer in some cases (Center of Food Safety 2023).

In commercial packed foods, chemicals, toxins and plastic components such as BPA may migrate from packaging materials to food, including packaging materials made from recycled paper that contain higher levels of benzophenone, each of which may be associated with an increased risk of certain cancers (Cooke and Mehta 2015; Fiolet et al. 2018).

In summary, fresh and natural products should be used as much as possible in preparing foods, and also, attention must be given to balancing the diet with respect to alkalizing and acidogenic effects according to the Warburg Hypothesis (Bahrami and Greiner 2021; Bahrami, Tafrihi, and Mohamadzadeh 2022).

TECHNICAL OVERVIEW

The metabolic wastes of different foods are transferred from the cells via venous blood; hence, venous blood gas (VBG) data can be used to measure this effect; while diet type does not significantly affect the arterial blood gas (ABG) data (Wu et al. 2019; Kreuzer 2020; Higgins 2011).

A VBG test can address acid-base imbalances such as alkalosis when blood pH is higher than the normal level, acidosis when blood pH is lower than the normal level, or compensated acidosis in which the pH of the venous blood appears normal, but there are higher than normal levels of bicarbonate in the blood that has compensated for earlier acidosis (Bahrami and Greiner 2021).

Using VBG data, oxygen saturation (%) can also be estimated, another key indicator regarding acid-base imbalance, using the following equation ("PO2 and Calculated Oxygen Saturation" 2003; Chetana Shanmukhappa and Lokeshwaran 2023):

$$Oxygen\ Saturation = 100 * \frac{X^3 + (150 * X)}{X^3 + (150 * X) + 23400}$$

Where $X = P\left(O_2\right) * 10^{0.48*(pH-7.40)-0.0013*(HCO3-25)}$

& $pH = -Log(concentration\ of\ hydrogen\ ions\ [H^+])$

In addition, VBG analysis can determine acid-base status by calculating base excess (BE), which can be calculated from BE = 0.9287* (HCO_3^- − 24.4) + 13.77*(pH − 7.40), showing the amount of base present in the venous blood (Singh, Khatana, and Gupta 2013; Taussig and Landau 2008; Morgan 2018).

As reference values for VBG analysis, oxygen saturation in the range of 65-80% is normal/ideal, around 30-50% may be considered as moderate oxygen levels (indicates an increase in O2 demand), down to 25-30% may indicate oxygen deficiency (indicates the beginning of lactic acidosis), and less than 25% is extreme oxygen deficiency (indi-

Table 1. Acidogenic or alkalizing effects for certain foods (Bahrami and Greiner 2021; Bahrami, Tafrihi, and Mohamadzadeh 2022)

Category	Acidifier (Positive Dietary Acid Load)			Alkalizer (Negative Dietary Acid Load)		
	Strong	Medium	Weak	Weak	Medium	Strong
Fruits	Prunes, Canned fruits, Industrial juices	Sour cherry, Sour plum, Unripen fruits	Sweet plums	Oranges, Bananas, Cherries, Peaches, Pomegranates	Grapes, Apples, Pears, Melons, Raisins,	Lemons, Dates, Figs, Mangoes
Vegetables, Beans, Legumes	Fried potatoes, Chips, Pickled vegetables	Lima beans, Peas, Lentils, Boiled potatoes, Tofu	Kidney beans, Some cooked vegetables	Cucumbers, Carrots, Tomatoes, Mushrooms Cabbage, Green peas	Olives, Green Beans, Okra, Turnips, Celery, Pumpkin, Bell peppers	Garlic, Onions, Spinach
Nuts and Seeds	Peanuts, Cashews	Walnuts, Pistachios	Seeds of Pumpkin, Sunflower, Sesame	-	-	Raw almonds
Meats	Pork, Shellfish, Rabbit	Beef, Lamb Turkey, Veal	Fish, Chicken	-	-	-
Eggs and Dairy	Cream, Ice Cream	Homogenized cow's milk, Cheese, Industrial eggs	Yogurt, Raw milk, Farm eggs	-	-	-
Grains and Cereals	Pastries, Pasta, Cereals	White rice, White flour, Oats, Bread	Whole wheat, Brown rice	-	-	-
Oils	Frying Oils	Sunflower oil, Sesame oil	-	-	-	Virgin olive oil
Drinks	Liquor, Beer, Most soft drinks,	Green Tea, Black Tea, Coffee, Wine	Bottled water	Spring mineral water, Fresh ginger tea, Fresh quince tea	Lemon juice, other fresh fruit juices, Fresh vegetable juices	-
Other foods	Chocolate, Ketchup, Mayonnaise, Protein shakes	Jam, Sugar, Vinegar	Processed Honey	Ginger, Natural honey	-	-

cates severe lactic acidosis) (Chetana Shanmukhappa and Lokeshwaran 2023; Dixon, Miller, and Scott 1984; Apatean et al. 2019; Marx et al. 1973). The normal range for BE is from -2 to +2 (near zero shows acid-base balance), a positive BE higher than +2 indicates too much base in the blood (metabolic alkalosis), and a negative BE lower than -2 is a sign of severe base deficit (metabolic acidosis). Venous blood pH of 7.33-7.42 is normal (7.37-7.40 is optimal), while less than 7.29 indicates acidosis, and lower than 7.0 means extreme acidosis. As the pH scale is logarithmic, even relatively small variations outside the normal range can have deleterious effects. For instance, a change in blood pH from 7.40 to 7.20 means 58% higher concentration of hydrogen ions (Bahrami and Greiner 2021; Dixon, Miller, and Scott 1984; Apatean et al. 2019; Marx et al. 1973).

The venous blood pH and oxygen saturation along with other related parameters such as BE, are useful for evaluating the acid-base balance of the blood, not limited to acidosis and hypoxia, but also the potential risks for several other physical problems such as cysts, tumors, type 2 diabetes, osteoporosis, formation of kidney stones, and possibly migraine-like headaches (Bahrami and Greiner 2021; Dixon, Miller, and Scott 1984; Apatean et al. 2019; Marx et al. 1973; Barar and Omidi 2013).

In summary, while diet and so-called dietary acid load have a significant effect on what have traditionally been called acid-base disorders and various disease states, including cancer, the effect has been poorly investigated. Our hypothesis was that adherence for 1-3 months to a well-balanced alkalizing diet (using Table 1 as a guide) would result in improving blood pH and other related parameters from VBG measurements. In a previous study (Bahrami and Greiner 2021), we discussed in detail the possible mechanisms behind the Warburg Effect and one of us (HB) tested an alkalizing diet on himself based on Table 1, finding that it had the expected effect on blood gas parameters, particularly venous blood pH and oxygen saturation. Here we report on results from a total of 10 individuals who adhered to such a diet.

METHODS

A VBG test was initially performed, then the dietary habits were modified and regularly monitored in an attempt to maintain adherence to this diet modification. After 1-3 months of consuming a prescribed alkalizing diet, VBG tests were repeated, under the same conditions and using the same methods and laboratory.

PARTICIPANTS

A total of 30 people volunteered to participate in this exploratory pilot study. Background information about these participants is reported in Table 2. Each participant first visited a medical doctor, explaining the study and requesting him to order VBG measurements. Then each did the VBG test in a reliable, certified laboratory. After that, the participants were given general guidelines for preparing alkalizing meals and maintaining healthy dietary habits (Bahrami 2023) and were requested to follow the diet plan for a duration of 1-3 months or more between two blood draws.

During the modified diet period, they were requested to increase their daily intake of alkalizing foods such as raw almond, date fruits, fresh raw vegetables, and plant-based foods such as green beans; as well as to significantly reduce their intake of acidogenic foods such as milk, fried foods, red meats, chocolates, pastries, and fast foods, as well as also avoid caffeine, cigarettes, carbonated soft drinks, alcohol, and to abstain from taking vitamin/mineral supplements. Only 10 participants completed the diet for the requested period. Their diet was modified and supervised by one author (HB). They were the only ones who received a second VBG measurement.

The alkalizing diet was planned for each participant, or each group of participants, in such a way that it was as close to their usual diet as possible so that it could be implemented over the long-term. First, detailed information about their usual diet was obtained, and then diet modification which included sufficient amounts of alkalizing foods was discussed with each individual or family.

For example, someone whose lunch consisted mainly of rice and meat (both acidifying) would switch to rice and less meat, but add plant foods such as cooked green beans, carrots, tomatoes, and fresh onions, cooked in boiling water with a little pure powder of black pepper and turmeric. In addition, they were advised to add olive oil on the rice and a little fresh lemon juice on the stew, to make the meal more effectively alkalizing. Also, biscuits or chocolates as a snack were replaced with dates with raw almonds or fresh fruit.

Replacement foods were based on a list of foods that each participant provided as preferred food choices beforehand, and the foods that they did not like were not included to the modified diet. This allowed the participants to follow the modified diet for a long period of time without getting bored with the foods. For example, Participant #2, who had been diagnosed with cancer and was under medical treatment, after following the alkalizing diet that was specifically prepared for her, experienced a significant health improvement. Satisfied with these results, she has been following this diet for about 3 years to date.

BLOOD GAS ANALYSIS

Blood samples were taken from the median cubital vein. Analysis was performed immediately in a Blood Gas Analyzer (Farabi Medical Laboratory, n.d.) (a product of OPTI Medical Systems, Inc ["OPTI CCA-TS2 Blood Gas and Electrolyte Analyzer," n.d.]., model OPTI CCA-TS2). The sample was checked/evaluated for at least 10 minutes to ensure the accuracy of the result. Oxygen saturation (SO_2) and base excess (BE) values were calculated using the reference correlations (Farabi Medical Laboratory, n.d.).

STATISTICS

Data were analyzed using the SPSS Statistical Package and the R software package. Before and after dietary modification data were compared using Paired Samples T-Tests. Due to the small sample size (10 participants), Wilcoxon Signed Ranks Test in SPSS and also Bootstrapped Paired T-Test with 10000 bootstrap replicates in the R software were also used. A p-value < 0.05 was considered to be statistically significant.

ETHICS

Participants gave informed consent and were informed that they could withdraw from the study at any time for any reason without consequence. A certificate of ethical approval for the study was obtained from the Research Ethics Committees of University of Mazandaran in Iran (Approval ID: IR.UMZ.REC.1402.028).

RESULTS

Table 2 provides an overview of the participants, some background information about them, and, for each, whether there was a supervised adherence to the diet for at least one month. As can be seen, having a diet-related non-communicable disease (NCD) or other health problem was closely associated with adherence. 6/10 of those who adhered had such a health problem, while this was the case for only 1/20 of those who did not adhere to the diet and/or did not consent to a second blood draw.

Table 3 provides the baseline VBG data for all 30 participants. These represent the key blood parameters related to the Warburg effect, i.e., blood pH, oxygen saturation, partial pressure of carbon dioxide, and bicarbonates level, along with the reference ranges.

Figure 1 is based on blood pH data only from the 10 participants who adhered to the diet and provided blood both before and after the diet period. Results from three different statistical approaches are provided, all finding that

Table 2. Background information on the participants in this study

No.	Gender	Age group	Health Status / Disease	Followed a supervised alkalizing diet?	Alkalizing diet duration (The period of time between the two blood draws)
1 (HB)	Male	30-40	No major NCDs	Yes	1 month
2	Female	60-70	Breast cancer (Stage 3)	Yes	3 months
3	Male	60-70	Kidney cysts	Yes	3 months
4	Female	30-40	Breast cysts	Yes	3 months
5	Female	30-40	No major NCDs	Yes	3 months
6	Female	50-60	Breast Cancer (Stage 2)	Yes	2 months
7	Female	20-30	Migraine	Yes	4 months
8	Male	30-40	No major NCDs	Yes	2 months
9	Male	20-30	No major NCDs	Yes	2 months
10	Female	40-50	No major NCDs	Yes	1 month
11	Female	50-60	Breast cancer (Stage 3)	No	-
12	Male	30-40	No major NCDs	No	-
13	Male	40-50	No major NCDs	No	-
14	Male	40-50	No major NCDs	No	-
15	Female	30-40	No major NCDs	No	-
16	Female	40-50	No major NCDs	No	-
17	Male	30-40	No major NCDs	No	-
18	Female	30-40	No major NCDs	No	-
19	Male	1-10	No major NCDs	No	-
20	Female	40-50	No major NCDs	No	-
21	Female	40-50	No major NCDs	No	-
22	Female	40-50	No major NCDs	No	-
23	Male	30-40	No major NCDs	No	-
24	Male	30-40	No major NCDs	No	-
25	Male	40-50	No major NCDs	No	-
26	Male	30-40	No major NCDs	No	-
27	Male	40-50	No major NCDs	No	-
28	Female	40-50	No major NCDs	No	-
29	Male	30-40	No major NCDs	No	-
30	Female	10-20	No major NCDs	No	-

there was a significant change in the pH of the venous blood before and after the diet period (p-value < 0.05). Thus, the diet had the effect of increasing the 'mean pH' from a state of acidosis to the optimal range (7.25 before and 7.40 after).

The calculated BE values show that 8 of the 10 participants were initially out of the normal range, but following the alkalizing diet, 7 of 10 were improved towards the normal range, suggesting that the individualized alkalizing diet plans used could increase the deficient amounts of base present in the blood (However, in one case there was a decrease). Furthermore, two participants, one normal and the other with acidosis at baseline, had an increase of BE values to values that were too high (alkalosis) after the dietary period, indicating that there may be a risk of following a diet that is too extreme, that is, contained too much alkalizing food.

DISCUSSION

Several studies have proposed diet-based strategies for cancer control based on the Warburg effect, but they have had significant limitations and failed to achieve satisfactory results. For instance, calorie restriction by fasting has been proposed as a method to reduce glucose uptake by cancer cells (Tran et al. 2020), which may not be suitable for all cancer patients, especially those weakened by the cancer itself or by medical treatment. Ketogenic diets have also

Table 3. Baseline venous blood gas (VBG) blood examination results for all subjects

Participants	Blood pH		O_2 Saturation %		HCO_3^- mmol/L		P CO_2 mmHg		Base Excess (BE), mEq/L	
	Before	After	Before	After	Before	After	Before	After	Before	After
1	7.30	7.42	31	81	23	24	**53**	35	-2.7	-0.1
2[a]	**6.86**	7.43	46	63	22	25	**53**	38	-9.7	1.0
3[a]	**7.20**	**7.46**	72	80	23	**20**	**51**	29	-4.1	-3.3
4[a]	**7.24**	7.42	58	43	23	25	**51**	40	-3.5	0.8
5[a]	7.31	7.41	72	60	24	25	45	40	-1.6	0.7
6	7.35	7.34	**21**	45	21	25	38	48	-3.8	-0.3
7	7.32	7.38	**21**	34	22	25	44	44	-3.3	0.3
8	7.42	7.35	46	76	28	24	45	34	3.6	-1.1
9[b]	**7.26**	7.36	34	46	24	**34**	**55**	**60**	-2.3	8.4
10[c]	7.34	7.37	37	38	24	28	47	49	-1.2	2.9
11	7.23	NA	**22**	NA	19	NA	46	NA	-7.4	NA
12	7.37	NA	36	NA	27	NA	46	NA	2.0	NA
13	7.37	NA	**29**	NA	32	NA	**56**	NA	6.6	NA
14	7.39	NA	67	NA	34	NA	**58**	NA	8.8	NA
15	**7.45**	NA	89	NA	22	NA	30	NA	-1.5	NA
16	7.38	NA	74	NA	17	NA	28	NA	-7.1	NA
17	7.37	NA	58	NA	24	NA	42	NA	-0.8	NA
18	7.37	NA	**25**	NA	22	NA	39	NA	-2.6	NA
19	7.31	NA	66	NA	24	NA	47	NA	-1.6	NA
20[d]	7.41	NA	41	NA	22	NA	35	NA	-2.1	NA
21[d]	7.40	NA	57	NA	26	NA	42	NA	1.5	NA
22[d]	7.33	NA	30	NA	25	NA	47	NA	-0.4	NA
23	7.35	NA	80	NA	23	NA	41	NA	-2.0	NA
24	7.32	NA	31	NA	24	NA	47	NA	-1.5	NA
25	7.34	NA	40	NA	25	NA	48	NA	-0.3	NA
26	7.33	NA	**29**	NA	26	NA	**50**	NA	0.5	NA
27	7.39	NA	58	NA	29	NA	48	NA	4.1	NA
28	7.37	NA	53	NA	26	NA	44	NA	1.1	NA
29	7.37	NA	55	NA	24	NA	42	NA	-1.0	NA
30	7.42	NA	64	NA	21	NA	33	NA	-2.8	NA
Reference range values (Bahrami and Greiner 2021; Taussig and Landau 2008; Morgan 2018; Dixon, Miller, and Scott 1984)	7.33 - 7.42		65–80 %		22 - 28		35-46		-2 to +2	

Bold numbers indicate values that are outside a normal range;

[a]From the same family who did their VBG tests in the same laboratory at the same time

[b] Walked for nearly an hour before both VBG tests

[c]A less-adherent participant who occasionally considered the alkalizing the diet, but did not always follow the diet plan accurately

[d]Members of another family who did their baseline VBG test in the same laboratory at the same time

been proposed, which limit sugar consumption and include high amounts of fat and moderate amounts of protein in the diet (Tran et al. 2020), but such diets have largely failed to treat cancers. This may be because cancer cells can eventually adapt to using fats for energy. In addition, some food we theorize to be useful in preventing and treating cancer, such as fruits, are restricted in ketogenic diet. In addition, the ketogenic diet includes animal foods that are acidogenic and a major risk factor for cancer according to the Warburg Hypothesis. Hence, some have warned against using the ketogenic diet for either cancer prevention or cancer treatment (Bahrami, Tafrihi, and Mohamadzadeh 2022; Mawer 2021).

As Warburg suggested that oxygen deficiency at the cell level increases the risk of cancer, oxygen therapies and hyperbaric oxygen treatment have been tested to increase oxygenation of body tissues. However, they have had only temporary effects without much benefit in treating cancer (Bahrami and Greiner 2021; Moen and Stuhr 2012; Bennett et al. 2018). As previously discussed, the alkaline-water or baking soda (sodium bicarbonate) that are advertised as body alkalizers are based on a misunderstanding of the

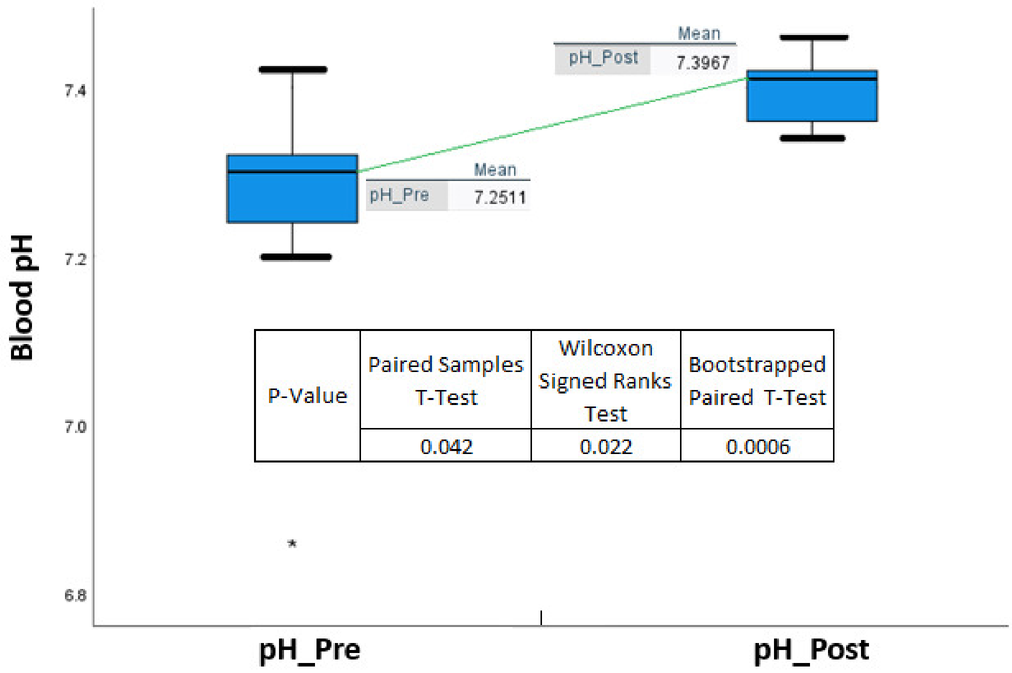

Figure 1. Mean (±SD) venous blood pH before (pH-Pre) and after (pH-after) 1-4 months of adherence to an alkalizing diet

The thick horizontal black lines represent the range and the asterisk represents an outlier.

Warburg Hypothesis, and alkaline water also had no effect in preventing or treating cancer (ASCO 2021).

An appropriate diet modification that includes a high intake of alkalizing foods such as fresh vegetables and fruits may be an effective way to control cancer. One study found that survival rates of cancer patients who had a higher intake of alkalizing foods diet was longer. They suggested that in addition to standard therapies, alkalization therapy may be associated with more favorable outcomes (Isowa et al. 2023).

Wada et al (Wada et al. 2022). provide a detailed description of how cancer causes its microenvironment to be acidic (as Warburg suggested), and that this in turn provides an environment in which cancer can proliferate. They theorize that alkalizing these areas could be accomplished through a particular diet. They hypothesized that it should be composed of fruits and vegetables, with no meat, and no dairy products. However, without a reliable/practical chart of alkalizing foods, they could find no way recommend a diet in more detail than this. In addition, they used a megadose of vitamin C to reduce inflammation. Using urine pH as their only indicator of success, they provide case studies of a few patients in which this therapy seemed to be beneficial (in conjunction with the usual cancer therapy).

Our study, with quantified results based on VBG analysis tests, suggest that the alkalizing diet may be effective in improving blood pH and oxygen saturation, i.e., factors that, according to the Warburg Hypothesis, may play a key role in initiation and development of various disease processes, including cancer. Further research should be done to determine whether a balanced, alkalizing diet could assist chemotherapies to control cancer more effectively, and/or to help cancer patients better recover from the side effects of medical treatments.

In the past, this kind of thinking has been restricted to tradition or complementary medicine. However, a recent line of modern scientific research may be converging with it, that is, research on the dietary causes and impact of inflammation (Malesza et al. 2021). The diets found to reduce systemic inflammation are similar to the one we studied here (Lankinen, Uusitupa, and Schwab 2019). Indeed, the process leading to and resulting from obesity, also linked to NCDs, involves low-grade chronic inflammatory signaling (Lecube and López-Cano 2019). Interestingly, the Warburg effect may thus explain what is often occurring in many inflammatory processes.

However, with respect to dietary treatment or management of cancer, scientific evidence is limited and a definitive consensus on this subject has not been established (Taylor et al. 2022). In a study performed on athletes, during exercise and then rest after, those who had high-protein diet (hypothesized to be acid-forming), temporarily had a lower venous blood pH, while those with a diet higher in fruits and vegetables (hypothesized to be alkaline-forming) had a higher blood pH (Hietavala, Stout, et al. 2014). However, we have not found any published research on long-term effects of diet on actual blood pH in relation to abnormal cell functions and growth such as in cysts and tumors. Most studies have not considered determining the effect of diet on the pH of the venous blood that carries cellular metabolic wastes, instead, have looked at the effect of diet on urine pH (Isowa et al. 2023; Wada et al. 2022), which is not an actual indicator of body pH and may sometimes even be misleading (Bahrami and Greiner 2021).

In general, there is a lack of scientific evidence concerning the effect of diet-based health practices on blood acidity and the risk of disease, including cancer. The present study was conducted in an effort to explore the hypothesized relationships between diet type, dietary acid load, and blood pH-related parameters. Due to financial and time limitations, as well as the challenges in maintaining the diet for an entire month, the number of volunteered participants in this study was very small. We hope this research will inspire larger scale and more detailed studies of the relationship between diet and VBG and eventually, its impact on the incidence, development, and treatment of disease.

LIMITATIONS

The present research work was done independently and was not a hospital-based study. Sample selection was not based on a defined sampling procedure. No selection criteria were initially considered for the participants.

While 10 participants completed the study, 20 dropped out, either not willing to continue following the supervised alkalizing diet or being unwilling to have a second VBG blood test. Note that preparing alkalizing foods as per the given instructions as well as visiting the specified laboratory to take their blood would not only have taken their time, but also cost them financially. We speculate that most of those whose first VBG test showed near normal results were not motivated to follow the diet to any great extent. Hence, after around 3 years of follow up, the only 10 participants provided the before and after data points needed for the analysis.

CONCLUSIONS

Our findings suggest that diet could significantly affect pH, oxygen saturation, and other blood gas parameters of the venous blood. We hypothesize that this is due to diet-related metabolic wastes at cellular level excreted into the veins. Thus, we would argue that a balanced alkalizing diet may help to lower dietary acid load and maintain acid-base balance as well as improve oxygenation at the cellular level. This in turn may reduce the risk of various diseases, including cancer initiation in the hypoxic regions of the body. We further hypothesize that venous blood gas data concerning blood pH, oxygen saturation, bicarbonates level, and partial pressure of carbon dioxide, may indicate acid-base disorders at cellular level. Further research may prove this to be useful as a predictor of risk of various diseases and cancers.

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