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COMPARABILITY OF HBA1C AND LIPIDS MEASURED WITH DRIED BLOOD SPOT VERSUS VENOUS SAMPLES: A SYSTEMATIC REVIEW

Fredrica*

*Faculty of Medicine, Maranatha Christian University, Indonesia

***Corresponding Author:-**
fredricadr@gmail.com

Abstract

Diabetes is a major risk factor for cardiovascular disease, which is spreading at an alarming rate over the world, but it is especially widespread in developing nations. The infrastructure and resources required to conduct research are frequently insufficient in these countries, making it difficult to establish the role that dysglycemia and other metabolic risk factors play. DBS samples are now routinely used to evaluate serum antibodies, human immunodeficiency virus (HIV) loads, and blood hormone levels. There is enough evidence to prove the comparability of results between research using DBS samples and those using conventional venous samples. The DBS method appears to hold significant potential for addressing the logistical challenges of venous sampling for research of metabolic risks in resource-constrained situations, but only if standards and calibrations can be agreed upon, as has been done in other fields of study. As a result of the breadth of comparisons provided by our findings, we may conclude that these generalizations are true of data acquired from a variety of different laboratories. There have been reports in the scientific literature concerning findings that are equivalent in terms of the strength of the linkages between DBS assay values and venous sample values. Tests based on DBS samples are clearly related with assays based on standard venous samples for HbA1c and selected blood lipids.

Keyword: *Dried Blood Spot; HbA1c; Lipids; Venous*

INTRODUCTION

Coronary heart disease (CHD) has developed as a useful operational term that refers to a spectrum of conditions compatible with acute myocardial ischemia and/or infarction that are usually caused by a sudden reduction in coronary blood flow.[1,2] According to the World Health Organization (WHO), cardiovascular disease is the main cause of death from PTM and causes 17.5 million deaths or 46% of all deaths from non-communicable diseases, 80% occur in countries with lower middle income, and this figure is expected to increase to 23.6 million in 2030. The data estimates that 7.4 million deaths will be heart attacks due to CHD and 6.7 million will be strokes.[3]

Diabetes is a critical risk factor for cardiovascular disease, which is expanding at an alarming rate worldwide, but it is especially prevalent in poorer countries. In these nations, the infrastructure and resources necessary to carry out research are often lacking, making it difficult to document the role that dysglycemia and other metabolic risk factors play.[4,5] Analyses of glycosylated haemoglobin (also known as HbA1c) and blood lipids, for instance, are often performed on samples of venous blood, which can be challenging to collect, transport, and preserve.[6,7]

One potential approach is the use of dried blood spot sampling, also known as DBS. The participant's finger is pricked with a lancet during the DBS procedure, and then a few drops of their blood are collected on a piece of filter paper. After being washed and allowed to air-dry, samples are packaged for transport and long-term storage in airtight plastic bags. When compared to the collection of venous samples, the collection of DBS samples involves much less training of staff, is less expensive, poses less health risks, facilitates easier transportation, and is preferred by research participants.[7,8]

DBS samples are now commonly utilized for assessing serum antibodies, human immunodeficiency virus (HIV) loads, and blood hormone levels. There are sufficient amounts of data to establish the comparability of results between studies based upon DBS samples and standard venous samples.[9] Because there is a lack of comparable data to identify the connections for HbA1c and blood lipids, DBS samples are not commonly used in studies that examine the potential for cardiovascular hazards.[8,10] In this study, a comparison is made between measuring HbA1c and lipids with dried blood spots and with venous samples.

METHODS

Protocol

The methodology of this inquiry was carried out in accordance with the guidelines established by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. These factors had an impact on the decision to pass the legislation.

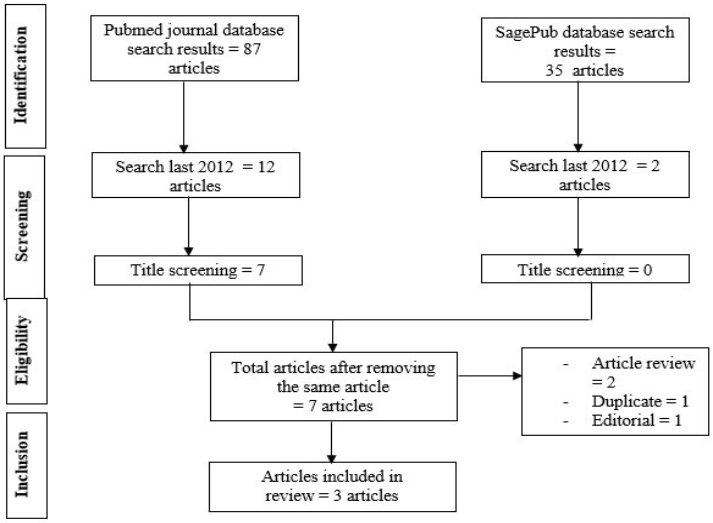

Figure 1. Article search flowchart

Criteria for Eligibility

By assessing or analyzing previous research on the subject, this review of the literature aims to compare of HbA1c and lipids measured with dried blood spot versus venous samples. This is a major concern raised in the current study. Researchers take part in studies that meet the following criteria: 1) To be considered for publication, articles must be written in English and highlight or focus on compare of HbA1c and lipids measured with dried blood spot versus venous samples. 2) This evaluation included articles published after 2015 but before the period covered by this systematic review. Editorials, submissions without a DOI, previously published review articles, or entries that are very similar to those previously published in a journal, for example, will not be considered for publication.

Search Strategy

The search for studies to be included in the systematic review was carried out from September, 22th 2022 using the PubMed and SagePub databases by inputting the words: “HbA1c”; “lipids”; “blood spot”, and “venous samples. Where *("glycated hemoglobin"[MeSH Terms] OR ("glycated"[All Fields] AND "hemoglobin"[All Fields]) OR "glycated hemoglobin"[All*

Fields] OR "hba1c"[All Fields] OR "hba1cs"[All Fields]) AND ("lipid s"[All Fields] OR "lipidate"[All Fields] OR "lipidated"[All Fields] OR "lipidates"[All Fields] OR "lipidation"[All Fields] OR "lipidations"[All Fields] OR "lipide"[All Fields] OR "lipides"[All Fields] OR "lipidic"[All Fields] OR "lipids"[MeSH Terms] OR "lipids"[All Fields] OR "lipid"[All Fields]) AND ("blood"[MeSH Subheading] OR "blood"[All Fields] OR "blood"[MeSH Terms] OR "bloods"[All Fields] OR "haematology"[All Fields] OR "hematology"[MeSH Terms] OR "hematology"[All Fields] OR "haematoma"[All Fields] OR "hematoma"[MeSH Terms] OR "hematoma"[All Fields] OR "haemorrhage"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "haemorrhages"[All Fields] OR "hemorrhages"[All Fields] OR "haemorrhagic"[All Fields] OR "haemorrhaging"[All Fields] OR "hematologies"[All Fields] OR "haematomas"[All Fields] OR "hematomas"[All Fields] OR "hematoma s"[All Fields] OR "hematomae"[All Fields] OR "hemorrhaged"[All Fields] OR "hemorrhagic"[All Fields] OR "hemorrhagical"[All Fields] OR "hemorrhaging"[All Fields]) AND "spot"[All Fields] AND ("veins"[MeSH Terms] OR "veins"[All Fields] OR "venous"[All Fields]) AND ("sample"[All Fields] OR "sample s"[All Fields] OR "sampled"[All Fields] OR "samples"[All Fields] OR "sampling"[All Fields] OR "samplings"[All Fields]) is used as search keywords.

Data retrieval

The author revised the inclusion and exclusion criteria after completing a literature review that included an examination of the titles and abstracts of previously conducted research. The study's supplementary materials include an explanation of the newly developed criteria. This brought to light the various aspects of the problem that require further investigation, as well as the scope of the problem. The author reached this conclusion after conducting research on a wide range of other studies that followed a similar format. Only papers that met all of the inclusion criteria were taken into account during the systematic review process.

This ensured that during the search, only relevant information was discovered. Our team did not consider research proposals that did not meet all of our requirements for evaluation. As a result, it was ensured that a thorough evaluation would be carried out. This effort yielded information pertinent to the studies, such as their titles, authors, publication dates, locations, types of research investigations, and parameters. These are the various product categories that are readily available. These are skills that can be developed with practice. Depending on the source of the information, this information could be provided in a variety of formats.

Quality Assessment and Data Synthesis

Before deciding which articles to investigate, each author conducted an independent investigation of a piece of research mentioned in the titles and abstracts of the papers. The full texts of publications that meet the systematic review's inclusion criteria will then be reviewed to determine which papers will be included in the review. This determines which articles will be reviewed. To facilitate the selection of articles for the review. Which studies are of sufficient quality to be included in the review?

RESULT

Crimmins, et al (2014)[11] showed DBS method results in values that have a good correlation with levels of whole blood HbA1c, cystatin C, and C-reactive protein. It would suggest that determining accurate lipid levels with DBS is a more difficult challenge. However, even when the values obtained from DBS and those obtained from venous blood are highly linked, they are frequently on different scales; as a result, employing standard cutoffs may be deceptive. Moreover, even when the values obtained from DBS and those obtained from venous blood are highly linked, they are frequently on different scales.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Period	Result
Crimmins, 2014[11]	United States ofAmerica (USA)	Cross sectional study	92 volunteer subjects	June through December 2010	The DBS method yields values that are strongly related to HbA1c, cystatin C, and C-reactive protein levels in whole blood. Assessing lipid levels with DBS appears to be more difficult. Even when DBS values and venous blood values are highly correlated, they are frequently on different scales, and using conventional cutoffs may be misleading.
Mastronardi, 2015[12]	Australia	Cross sectional study	Eleven and 56 patients had type 1 and type 2 diabetes mellitus	No data	On all days, the median intra-assay CV for WB and capDBS was less than 3%. According to Bland-Altman plots, data from capDBS and venDBS showed strong correlation and agreement to WB results, with narrow 95% limits of agreement (except for results from D14 samples). When capDBS values were applied to regression models, the results were similar to WB values. A cross-validation model revealed that capDBS results on D0, D4, and D7 were comparable to WB results, with prediction ranges that were clinically acceptable.
Börsch-Supan, 2021[13]	Germany	Cross sectional study	20 donors	July 20 to 30, 2018	The DBS analyte levels are significantly impacted by the field conditions as well as the sample quality, and this influence varies from test to assay. The most significant problem is the variable spot size, which has an effect on all markers other than HbA1c. When measured, smaller patches result in significantly higher amounts.

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The DBS analyte levels are significantly impacted by the field conditions as well as the sample quality, and this influence varies from test to assay. The most significant problem is the variable spot size, which has an effect on all markers other than HbA1c. When measured, smaller patches result in significantly higher amounts. A lack of desiccant had a negative impact on all indicators with the exception of CRP and tHb. When it comes to HDL and CysC, the temperature to which the samples are subjected plays a significant role; on the other hand, a drying period that is too short has an effect on CRP and CysC. Adjustment equations developed in the lab that take into consideration the variations between re-liquefied DBS and venous blood do not take into account the conditions that are present in the field.[13]

DISCUSSION

According to the World Health Organization (WHO), cardiovascular disease is the main cause of death from NCD and causes 17.5 million deaths or 46% of all deaths from non-communicable diseases, 80% occur in countries with lower middle income, and this figure is expected to increase to 23.6 million in 2030. The data estimates that 7.4 million deaths will be heart attacks due to CHD and 6.7 million will be strokes. Broadly speaking, CHD risk factors can be divided into two. First are risk factors that can be repaired (reversible) or can be modified (modifiable), namely: Dyslipidemia (raised LDL, decreased HDL), Smoking, Hypertension, Diabetes Mellitus, Metabolic Syndrome, Lack of physical activity. While risk factors that cannot be corrected include: Old age, gender, and heredity.[3]

The association between diabetic, dyslipidemia, and heart disease is well established. Arteries are blood vessels that function to carry blood that functions to carry blood from the heart throughout the body. Arteries have a thin lining on the inside called the endothelium. This layer is responsible for keeping the inside of the arteries healthy and smooth, so that blood can flow smoothly. Dyslipidemia can cause CHD because in dyslipidemia there is an increase in the concentration of LDL cholesterol, triglycerides, total cholesterol, and a decrease in HDL cholesterol which are anti-atherogenic, anti-oxidant and anti-inflammatory, where the whole process will reduce natural anti-oxidant reserves. This antioxidant deficiency condition will make blood vessels more susceptible to endothelial injury, which is the forerunner of atherosclerosis in CHD.[14,15]

Previous data provide a strong rationale for the further investigation of DBS sample collection techniques and serve to highlight a number of areas that require further exploration before the method can be considered mainstream in this field. However, the data also serve to highlight a number of areas that provide a strong justification for the further investigation of DBS sample collection techniques. The DBS method does appear to have substantial promise to address the logistical issues of venous sampling for studies of metabolic hazards in settings with limited resources, but only if standards and calibrations can be agreed upon, as has been accomplished in other areas of study.[9]

A substitute for the more common practice of taking blood samples, the collection of dried blood spots has been put to use in clinical and epidemiological research for the better part of three decades. This method yields results that are comparable to those acquired from conventional venipuncture, but it does so without the logistical challenges that are associated with traditional venipuncture in terms of the collection, processing, transportation, and storage of samples. DBS has also been found to yield findings for the measurement of HbA1c that are comparable to those obtained from venous sampling.[16,17]

When the results of assays on DBS collected under conditions that are analogous to those that would be used in the field for large studies are compared with the results of assays performed on venous blood samples, it is found that there is a strong correlation between the levels of CRP, HbA1c, and cystatin C in venous blood. When compared to the levels found in venous blood, cholesterol measurements, whether for total cholesterol or HDL, tend to have a lower degree of reliability.[11,18,19]

The range of comparisons that our findings provide enables the study to reach the conclusion that these generalizations are true of the data acquired from a number of different laboratories. This is the conclusion that can be drawn from the study. There have been reports in the scientific literature about findings that are comparable regarding the strength of the connections between the values that were obtained from DBS assays and those that were obtained from venous samples. These reports have been made available online for anyone interested in reading them. These findings are relevant to a variety of CRP tests, as well as cholesterol and HbA1c.[11,19]

The discrepancies in the intercepts of the regression lines generated for the various analytic methods used for HbA1c assay demand careful study in terms of their significance. If the variation is related to the analytic method used, then a standard strategy for each analyte of interest must be recommended. However, while the analytic technique is the obvious explanation for the observed variation, it is not possible to rule out alternative reasons based on the available data. Other parts of the DBS sample preparation, including as transportation and extraction, were not standardised among the different analysis techniques, which may have contributed to the observed variations.

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In an actual situation, samples of DBS are either sent or delivered to the pathology laboratory that is responsible for performing the tests. As a consequence of this, DBS samples are not immediately analyzed. In order to determine whether the time that passed between data collection and analysis could have an impact on the findings, we did further analyses four, seven, and fourteen days after the acquisition of the data. We have shown that, as time passes, the correlation between the DBS and the venous blood findings becomes poorer, and the 95% limits of agreement increase larger. This is notably true for the D14 results, which may be clinically unsatisfactory.[20]

It is important to note that WB samples lose their quality with time if they are not analyzed right away, particularly if they are not stored in a refrigerator. In samples that have coagulated and matured, there is a possibility that haemoglobin breakdown products will be present. It is possible for these compounds to co-elute with HbA1c or for them to be incompletely separated from it. In these kinds of situations, the HbA1c result that is measured can end up being reported as being significantly higher than it actually is. This effect is especially noticeable in venDBS samples because those samples were taken without the use of an anticoagulant.[20]

CONCLUSION

Tests based on DBS samples are clearly related with assays based on standard venous samples for HbA1c and selected blood lipids.

REFERENCE

[1]. Zipes D, Libby P, Bonow R. Braunwald's Heart Disease. 8th ed. Philadelphia: Elsevier; 2019.

[2]. Ponikowski P; Voors AA; Anker SD; et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Eur Heart J. 2016;37(27):2129–200.

[3]. Cagle SD, Cooperstein N. Coronary Artery Disease: Diagnosis and Management. Prim Care. 2018;45(1):45–61.

[4]. Galiè N, Humbert M, Vachiery J-L, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016 Jan;37(1):67–119.

[5]. Lind L, Ingelsson M, Sundstrom J, Ärnlöv J. Impact of risk factors for major cardiovascular diseases: a comparison of life-time observational and Mendelian randomisation findings. Open Hear. 2021 Sep;8(2).

[6]. Brown AE, Walker M. Genetics of Insulin Resistance and the Metabolic Syndrome. Curr Cardiol Rep. 2016 Aug;18(8):75.

[7]. Jones TG, Warber KD, Roberts BD. Analysis of hemoglobin A1c from dried blood spot samples with the Tina-quantR II immunoturbidimetric method. J Diabetes Sci Technol. 2010 Mar;4(2):244–9.

[8]. Mei J V, Alexander JR, Adam BW, Hannon WH. Use of filter paper for the collection and analysis of human whole blood specimens. J Nutr. 2001;131(5):1631S-1636S.

[9]. Hamers RL, Smit PW, Stevens W, Schuurman R, Rinke de Wit TF. Dried fluid spots for HIV type-1 viral load and resistance genotyping: a systematic review. Antivir Ther. 2009;14(5):619–29.

[10]. McDade TW, Williams S, Snodgrass JJ. What a drop can do: dried blood spots as a minimally invasive method for integrating biomarkers into population-based research. Demography. 2007;44(4):899–925.

[11]. Crimmins E, Kim JK, McCreath H, Faul J, Weir D, Seeman T. Validation of blood-based assays using dried blood spots for use in large population studies. Biodemography Soc Biol. 2014;60(1):38–48.

[12]. Mastronardi CA, Whittle B, Tunningley R, Neeman T, Paz-Filho G. The use of dried blood spot sampling for the measurement of HbA1c: a cross-sectional study. BMC Clin Pathol. 2015;15(1):1–7.

[13]. Börsch-Supan A, Weiss LM, Börsch-Supan M, Potter AJ, Cofferen J, Kerschner E. Dried blood spot collection, sample quality, and fieldwork conditions: Structural validations for conversion into standard values. Am J Hum Biol. 2021;33(4):e23517.

[14]. Fauci AS, Jameson JL, Kasper D, et al. Harrison's Principles of Internal Medicine 19th Edition. New York: McGraw-Hill Education; 2018.

[15]. Price SA; Lorraine MW, Price SA LM, Price SA; Lorraine MW, Price SA LM. Patofisiologi Konsep Klinis Proses-Proses Penyakit. Jakarta: EGC; 2016.

[16]. Williams SR, McDade TW. The use of dried blood spot sampling in the national social life, health, and aging project. Journals Gerontol Ser B Psychol Sci Soc Sci. 2009;64(suppl_1):i131–6.

[17]. McDade TW. Development and validation of assay protocols for use with dried blood spot samples. Am J Hum Biol. 2014;26(1):1–9.

[18]. McDade TW, Burhop J, Dohnal J. High-sensitivity enzyme immunoassay for C-reactive protein in dried blood spots. Clin Chem. 2004;50(3):652–4.

[19]. Fokkema MR, Bakker AJ, de Boer F, Kooistra J, de Vries S, Wolthuis A. HbA1c measurements from dried blood spots: validation and patient satisfaction. Clin Chem Lab Med. 2009;47(10):1259–64.

[20]. Selvin E, Coresh J, Jordahl J, Boland L, Steffes MW. Stability of haemoglobin A1c (HbA1c) measurements from frozen whole blood samples stored for over a decade. Diabet Med. 2005;22(12):1726–30.