Research Article

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Comparison of Venous and Capillary Whole Blood Estimations of Covid-19 IgG and IgM Antibodies

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ABSTRACT

The testing of Covid-19 antibodies is fast becoming an important activity in the understanding and management of Covid-19 infection. Most of the tests are conducted on the venous blood samples. As quite a number of the tests being produced are point of care tests such as the lateral flow methods, finger prick or capillary samples are more convenient than venous samples. A prospective observational study was carried out on paired capillary and venous samples from 41 healthy blood donors using the Boditech iCHROMA FIA fluorescence immunoassay (FIA) method for measuring IgM and IgG. Whilst there was agreement between the IgM results of 31/41 (76%) of the capillary and venous blood samples, with a disagreement between the results of 10/41 (24%) of the capillary and venous blood samples. There was agreement between the IgG results of 39/41 (95%) of the capillary and venous blood samples, with a disagreement between the results of 2/41 (5%) of the capillary and venous blood samples. In conclusion, using capillary samples as an alternative method to venous whole blood for estimating and measuring the Covid-19 IgG antibodies are acceptable, whilst IgM antibody testing using capillary samples warrants careful interpretation.

INTRODUCTION

The detection of antibodies has been important in understanding the course of the Covid-19 infection. There have been a number of methods such as enzyme linked immunoassay (ELISA), chemiluminescence immunoassays (CMIA) using discrete and bench top analysers, we haves recently compared the Boditech iCHROMA a portable fluorescent immunoassay (FIA) method of measurement of Covid-19 IgG antibody with the Abbott Architect SARS-CoV-2 and found very good overall agreement of 95%, with a sensitivity of 100% and a specificity of 90% [1]. In addition, the Boditech iCHROMA was shown to have performed very well with external quality control material provided by the UK National Institute of Biological Standards and Control (NIBSC) [2]. Most of the tests have been conducted on serum or plasma from venous whole blood samples. Several the tests being produced are point of care tests such as the lateral flow methods require finger prick or capillary samples which are more convenient than venous samples this sampling. In a study, where a Covid-19 IgG enzyme linked immunoassay (ELISA) antibody assay was studied in plasma from venous blood samples that had been collected in lithium heparin tubes and matched with capillary blood samples collected in lithium heparin tubes, there was a very high measure of concordance (Cohen's kappa coefficient of >0.88) between the two sample groups, indicating that capillary blood sampling is a reliable venous blood sample alternative [3]. In another study, fingerstick plasma showed a 100% concordance (R2 = 0.997) with matched patient venous plasma using the Abbott Architect™ SARS-CoV-2 IgG assay (Anderson et al). In this prospective observational study on paired capillary and venous whole blood samples from 41 healthy blood donors, we studied using the Boditech iCHROMA fluorescence immunoassay (FIA) method for measuring Covid-19 IgM and IgG antibodies to determine the practical solution of using capillary whole blood samples to venous whole blood.

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MATERIALS AND METHODS

Study Participants

Forty-one subjects (23 males and 18 females aged between 19 and 57 years) from a blood donor panel obtained from Cambridge Biosciences were recruited to volunteer for this study. Cambridge Biosciences obtains fresh human blood service in partnership with London-based Research Donors, which is a HTA licensed and ISO 9001 2015 certified company with Research Ethics (REC) approval as a Research Tissue bank. All donors provided consented to use their blood samples for research. Donors of Human Biospecimens supplied by Cambridge Bioscience have consented to the use of their samples for biological research purposes.

Venous and Capillary Blood Collection

Trained staff at London based research donors collected approximately 10ml of venous whole blood into blood collection tubes (BD Vacutainer® treated with lithium heparin). Samples were aliquoted from the tube for IgG and IgM analysis using the Boditech iCHROMA method described later. Capillary blood samples were also collected from the volunteers by the staff into lithium heparin coated Microvette® 100 by Sarstedt. Samples were aliquoted from the tube for IgG and IgM analysis using the Boditech iCHROMA method described later.

Boditech iCHROMA Method Principle: The test uses a sandwich immunodetection method; fluorescence labelled conjugates in a dried detection buffer binds to antibody in sample, forming antibody-antigen complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized anti-human IgG on test strip. The more antigen-antibody complexes lead to stronger fluorescence signal by the detector antigen which is processed by iCHROMA. The iCHROMA processes the signal using a cut off index of 0.9-1.1, results <0.9 are interpreted as negative, results between 0.9 and 1.1 are interpreted as indeterminate and results >1.1 are interpreted as positive.

The paired capillary and venous samples were analysed using the Boditech iCHROMA Fluorescence Immunoassay (FIA) IgG assay described below:

a) Transfer 150µL of detector diluent using a pipette into the detector tube containing a granule. When the granule is completely dissolved it becomes the detection buffer.

b) Aspirate 10µL of whole blood/serum/plasma/control with a pipette, and add into the detector tube, close and shake the tube at least 10 times.

c) Pipette out 75µL of the content of the tube and load it into the sample well on the test cartridge and leave or 10 minutes.

d) Insert the test cartridge into the cartridge holder in iCHROMA II device and press start

e) Read the result on the display screen of the iCHROMA II device.

RESULTS

A total of 41 volunteers took part in this study, of which 23 (56%) were male and 18 (44%) females. The average age was 34 years with a range of 19-57 years.

Covid-19 IgG

Covid-19 IgG antibodies were estimated on 41 subjects venous whole blood samples collected in lithium heparin tubes, 14 of the 41 (34%) subject's samples were identified as Covid-19 IgG positive, 2 of the 41 (5%) as indeterminate and 25 of the 41 (61%) as Covid-19 IgG negative. Covid-19 IgG antibodies were estimated in 41 subject's capillary whole samples collected in lithium heparin tubes, 14 of the 41 (31%) subject's samples were identified as Covid-19 IgM positive, none of the 41 (2.4%) as indeterminate and 27 of the 41 (966%) as Covid-19 IgM negative (Table 1).

Table 1: Showing agreement of venous and capillary whole blood samples with Boditech iCHROMA Covid-19 IgG interpretation (positive, indeterminate, negative).

	Venous Whole Blood IgG	Capillary Whole Blood IgG
Positive	14	14
Indeterminate	2	0
Negative	25	27

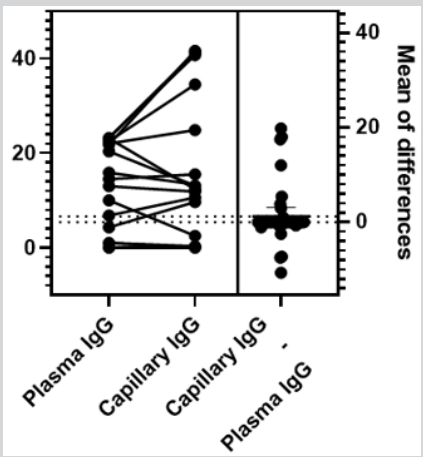

Figure 1: Showing cut off indices of Covid-19 IgG samples (capillary and venous whole blood).

The minimum, mean and maximum cut off indices of Covid-19 IgG detected in the venous whole blood samples were 0.00, 5.434 and 23.30 respectively, compared to minimum, mean and maximum cut off indices of Covid-19 IgG detected in the capillary whole blood samples was 0.00, 6,64 and 41.60 respectively. Paired T tests showed there was no significant difference (p=0.1968) between means of the IgG antibodies detected in the venous and the capillary whole blood samples (Figure 1).

There was concordance between the results of 39/41 (95%) of the capillary and venous blood samples, with a discordance between the results of 2/41 (5%) of the capillary and venous blood samples. The discordant samples (3643 and 3592), the cut off indices in the venous blood samples were 1.00, with the interpretation of indeterminate indicating a very low level of IgG antibodies were detected, their corresponding capillary blood sample was neagative (Table 2).

Table 2: Showing concordance of result interpretation of Boditech iCHROMA Covid-19 IgG using venous and capillary whole blood samples.

Volunteer No	Venous Blood IgG Cut Off Index	Interpretation	Capillary Blood IgG Cut Off Index	Interpretation
3423	21.8	Positive	41.6	Positive
3433	14.5	Positive	15.5	Positive
3431	4.3	Positive	9.7	Positive
3429	0	Negative	0	Negative
3435	0	Negative	0	Negative
3437	13	Positive	11.9	Positive
3427	0	Negative	0	Negative
3439	0	Negative	0	Negative
3429	23.2	Positive	40.7	Positive
3425	0	Negative	0	Negative
3640	0	Negative	0	Negative
3643	0	Negative	0	Negative
3645	1	Indeterminate	0.3	Negative
3657	0	Negative	0	Negative
3664	6.8	Positive	10.6	Positive
3660	0	Negative	0	Negative
3702	0	Negative	0	Negative
3704	22	Positive	24.9	Positive
3706	0	Negative	0	Negative
3708	0	Negative	0	Negative
3710	10	Positive	2.5	Positive
3718	0	Negative	0	Negative
3720	20.4	Positive	13.1	Positive
3726	0	Negative	0	Negative
3618	0	Negative	0	Negative
3592	0	Negative	0	Negative
3616	23.1	Positive	12.4	Positive
3584	1.01	Indeterminate	0	Negative
3581	0	Negative	0	Negative
3594	0	Negative	0	Negative
3590	0	Negative	0	Negative
3766	0	Positive	0	Positive
3775	23.3	Positive	41.3	Positive
3612	0	Negative	0	Negative
3598	0	Negative	0	Negative
3609	22.5	Positive	34.5	Positive
3771	0	Negative	0	Negative
3588	15.9	Positive	13.4	Positive
3622	0	Negative	0	Negative
3586	0	Negative	0	Negative
3773	0	Negative	0	Negative

Covid-19 IgM

Covid-19 IgM antibodies were estimated on 41 subjects venous whole blood samples collected in lithium heparin tubes, 11 of the 41 (27%) subject's samples were identified as Covid-19 IgM positive, 3 of the 41 (7%) as indeterminate and 27 of the 41 (66%) as Covid-19 IgM negative. Covid-19 IgM antibodies were estimated in 41 subject's capillary whole samples collected in lithium heparin tubes, 3 of the 41 (7.3%) subject's samples were identified as Covid-19 IgM positive, 1 of the 41 (2.4%) as indeterminate and 37 of the 41 (90.3%) as Covid-19 IgM negative.

The minimum, mean and maximum cut off indices of Covid-19 IgM detected in the venous whole blood samples were 0.00, 0.9588 and 5.20 respectively, compared to minimum, mean and maximum cut off indices of Covid-19 IgM detected in the capillary whole blood samples was 0.00, 0.4195 and 4.00 respectively. Paired T tests showed a significant difference ($p<0.0001$) between means of the IgM antibodies detected in the venous and the capillary whole blood samples (Figure 2).

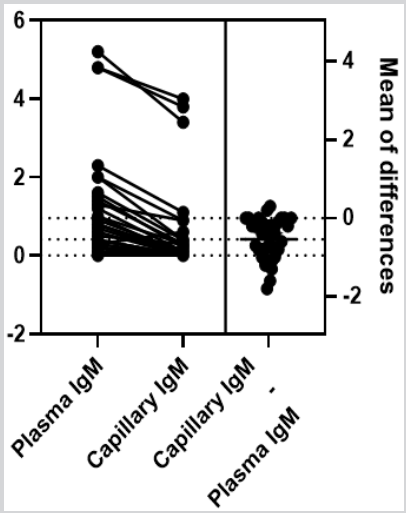

Figure 2: Showing cut off indices of Covid-19 IgM samples (capillary and venous whole blood).

There was concordance between the results of 31 of the 41 (76%) of the capillary blood and venous blood samples, with a discordance between the results of 10/41 (24%) of the capillary and venous blood samples. The discordant venous blood samples were indeterminate or positive with very low cut off indices (Table 3,4).

Table 3: Showing agreement of venous and capillary whole blood samples with Boditech iCHROMA Covid-19 IgM interpretation (positive, indeterminate, negative).

	Venous Whole Blood IgM	Capillary Whole Blood IgM
Positive	11	3
Indeterminate	3	1
Negative	27	37

Table4: Showing concordance of result cut off indices and interpretation of Boditech iCHROMA Covid-19 IgM using venous and capillary whole blood samples.

Volunteer No	Venous Blood IgM Cut Off Index	Interpretation	Capillary Blood IgM Cut Off Index	Interpretation
3423	0.3	Negative	0.6	Negative
3433	0.8	Negative	0	Negative
3431	0.4	Negative	0	Negative
3429	0.5	Negative	0.3	Negative
3435	0.8	Negative	0	Negative
3437	0.1	Negative	0.1	Negative
3427	4.8	Positive	4	Positive
3439	0	Negative	0.2	Negative
3429	2	Positive	0.9	Negative
3425	1.4	Positive	0.3	Negative
3640	1.2	Positive	0.1	Negative
3643	1	Indeterminate	0.3	Negative

3645	1.6	Positive	0.4	Negative
3657	0.2	Negative	0	Negative
3664	0.2	Negative	0	Negative
3660	0.3	Negative	0	Negative
3702	0.8	Negative	0.1	Negative
3704	1.3	Positive	0.9	Indeterminate
3706	0.2	Negative	0	Negative
3708	0.6	Negative	0	Negative
3710	0.7	Negative	0	Negative
3718	0	Negative	0	Negative
3720	0	Negative	0	Negative
3726	0.1	Negative	0	Negative
3618	5.2	Positive	3.4	Positive
3592	1	Indeterminate	0	Negative
3616	0.2	Negative	0	Negative
3584	0.8	Negative	0	Negative
3581	0.4	Negative	0	Negative
3594	0	Negative	0	Negative
3590	0	Negative	0	Negative
3766	2	Positive	0.4	Negative
3775	1.5	Positive	0.2	Negative
3612	0.91	Indeterminate	0.1	Negative
3598	0	Negative	0	Negative
3609	2.3	Positive	1.1	Positive
3771	0.2	Negative	0	Negative
3588	4.8	Positive	3.8	Positive
3622	0.4	Negative	0	Negative
3586	0.1	Negative	0	Negative
3773	0.2	Negative	0	Negative

DISCUSSION

In this study, there was a high level of agreement (95%) between the detection of Covid-19 IgG antibodies in venous and capillary whole blood samples. The discordance (5%) was seen in two venous whole blood samples that were interpreted as indeterminate indicating the presence of a low level of Covid-19 IgG antibodies in the venous whole blood samples the corresponding capillary blood samples were undetected and interpreted as negative and from the cut off indices had very low levels of Covid-19 IgG antibodies. The Covid-19 IgG antibody results in this study are consistent with findings in other studies, in which there was a concordance of >94% and a discordance of 2.4% between capillary and venous blood samples for Covid-19 IgG using an ELISA method [3]. Anderson et al. [4] also showed 100% concordance between fingerstick plasma and venous plasma on the Architect SARS-CoV-2 IgG assay.

There was a lower level of agreement (75%) for Covid-19 IgM antibodies between venous and capillary blood samples. This is much lower than what has been described by Anderson et al, where the concordance between plasma and venous or fingerstick dried bloods spots were 98.4% and 100%, respectively (Anderson et al). There is not much in the literature looking at the concordance of Covid-19 IgM antibodies between capillary and venous samples. A possible explanation for the higher discordance of IgM antibodies observed between the venous and capillary whole blood sample compared to IgG antibodies, could be as IgM is a larger molecule (molecular weight of 900kDa), compared to IgG which is much smaller molecule (molecular weight of 150kDa) and that is consistent with the results seen in this study, in which Covid-19 IgM antibodies were detected in 10 venous blood samples but not in the corresponding capillary blood samples [5-8].

CONCLUSION

our results indicate that capillary blood self-sampling is a reliable and feasible alternative to venepuncture for serological assessment in Covid-19 IgG antibodies and that the assessment of Covid-19 IgM antibodies be taken with some degree of caution.

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