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SYSTEMATIC REVIEW: BLOOD GLUCOSE CONCENTRATION DETERMINED FROM VENOUS AND CAPILLARY BLOOD SAMPLE

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Abstract: **Glucose can be measured as venous plasma or capillary whole blood. Capillary blood is more often used than venous blood in testing blood glucose concentration. Comparison of glucose concentration obtained from capillary blood and venous plasma blood is a wide topic of discussion, it varies the test result. The aim of the present study was to search and review the findings from the scientific published literature studies focusing on blood glucose concentration determined from venous and capillary blood sample. Of the 195 articles retrieved, in the final stage of the eligibility assessment, the remaining 7 studies were included in this review. The data obtained are in the form of descriptive analysis by narrating findings of scientific articles which are then arranged systematically and according to each topic discussed so that a conclusion is obtained that represents the entire content of the review. A good correlation between venous and capillary blood glucose resulted from this review. Although glucometers are useful, caution must be exercised in accepting the results in emergency hypoglycemic and hyperglycemia condition. Clinicians should always correlate the blood glucose reading in glucometers with the clinical findings in taking their management decisions.**

Keywords: **Blood Glucose Concentration, Venous, Capillary Blood Sample.**

I. INTRODUCTION

Early detection and intervention is crucial in diabetes management.[1] Many people with diabetes are required to regularly check their current glucose concentrations. Depending on their diabetes regimen, the glucose results can then be used to make therapeutic decisions, such as insulin dosing.[2] Blood glucose monitoring gives information on the glucose metabolism of the body, and monitoring a patient's blood glucose concentration is medically very important.[3]

The 2016 WHO global report on diabetes suggested that among the LMICs, only 1 in 3 have access to basic technologies which can help to diagnose and manage persons with diabetes. In primary care settings where laboratory analysis of venous plasma glucose is difficult, point of care testing (POCT) that measure glucose in capillary blood and meet ISO standards can be used for diagnosis of diabetes.[4]

Point-of-care testing (POCT) is defined as a laboratory test performed outside a central laboratory, usually at or near a clinical treatment site or by a patient. POCT capillary blood glucose (Glucometer) has been used for screening diabetes in low- and middle-income countries to decrease the disease burden. An advantage of using POCT is the rapid turnaround time (< 5 minutes vs at least 30 - 60 minutes), smaller sample size (usually glucometers need 0.3 - 1 µl of whole blood instead of 1 - 3 ml of serum/ plasma usually needed by clinical laboratories), automatic calibration, and minimal or simple maintenance.[5,6] Glucometers have a limited analytical measurement and can be inaccurate at the low and high blood glucose concentration. The International Organization for Standardization (ISO:15197:2013) recommends that 95% of glucometer results should be within ± 15 mg/dl when laboratory glucose concnentration are <100 mg/dl; and the acceptable error should be within ± 20% for laboratory concentration ≥100 mg/dl. ADA guidelines recommend an analytical error of ≤ 5% for all concentration.[7]

Glucose can be measured as venous plasma or capillary whole blood. Capillary blood is more often used than venous blood in testing blood glucose concentration for DM patient.[7] Comparison of glucose concentration obtained from capillary blood and venous plasma blood is a wide topic of discussion, it varies the test result.[3,7,8] The aim of the present study was to search and review the findings from the scientific published literature studies focusing on blood glucose concentration determined from venous and capillary blood sample.

II. MATERIALS AND METHODS

A. Protocol and Registration

A systematic review regarding to compare blood glucose concentration determined from venous and capillary blood sample.

Literature Tracing Strategy

The strategy used in finding articles is the PICOS framework, consists of:

- P (problem, patient, population) that will be analyzed based on this systematic review topic
- I (intervention, prognostic factor, exposure) is an action in the form of therapy given to cases in accordance with this systematic review topic
- C (comparison, control) is another action or intervention that is used as a comparison
- O (outcome) is the result or outcome obtained in previous studies in accordance with the topic of this systematic review
- S (study design) is a research design used by selected articles for further review

B. Keywords

The keywords used were: blood glucose concentration, venous, and capillary blood sample

C. Database or Search Engine

The data used in this research is secondary data obtained not from direct observation, but obtained from the results of research that has been conducted by researchers earlier. A comprehensive literature search conducted during November 2022 to Desember 2022 in the form of national and international articles using the database such as PubMed, Web Science, and Google Scholar

D. Inclusion and Exclusion Criteria

The inclusion and exclusion criteria used for this study have been presented in Table 1.

Table 1: PICOS framework criteria for systematic review of comparison blood glucose concentration determined from venous and capillary blood sample

PICOS	Inclusion Criteria	Exclution Criteria
Population	A national and international articles compare blood glucose concentration determined from venous and capillary blood sample	A national and international articles with design study systematic review, letter to editor, book, editorial Languages: other than Indonesia and English
Intervention	Blood glucose concentration determined from venous and capillary in human blood sample	Blood glucose concentration determined from arterious blood sample, and in animal blood sample
Comparation	The comparison were between blood glucose concentration determined from venous blood sample using autoanalyzer and blood glucose concentration determined from capillary blood sample using POCT (glucometer)	The comparison intervention groups used were between blood glucose concentration determined from venous blood sample and capillary blood sample using a single device (autoanalyzer or POCT (glucometer))
Outcome	Studies describe the comparison blood glucose concentration determined from venous and capillary blood sample	Studies that did not address the comparison to be observed
Study Design	Cross sectional study, prospective study, analytic description	Systematic review

In addition, the eligibility criteria are also used through the publication year of the articles used, namely 2017-2022 as inclusion criteria with national and international articles.

E. Data extraction, synthesis of the results and quality assessment

The title, abstract and the articles were reviewed independently. The information was taken from each study using a collection form that consisted of author, the publication year, title, method (design, sample, variable, instrument, type of data analysis), and results. This literature review is synthesized using the narrative method, did not use any other additional analysis techniques. The author only summarized the results in the literature then analyzed descriptively with a description in the form of a narrative explanation. The quality assessment for each selected study was conducted using the PRISMA method.

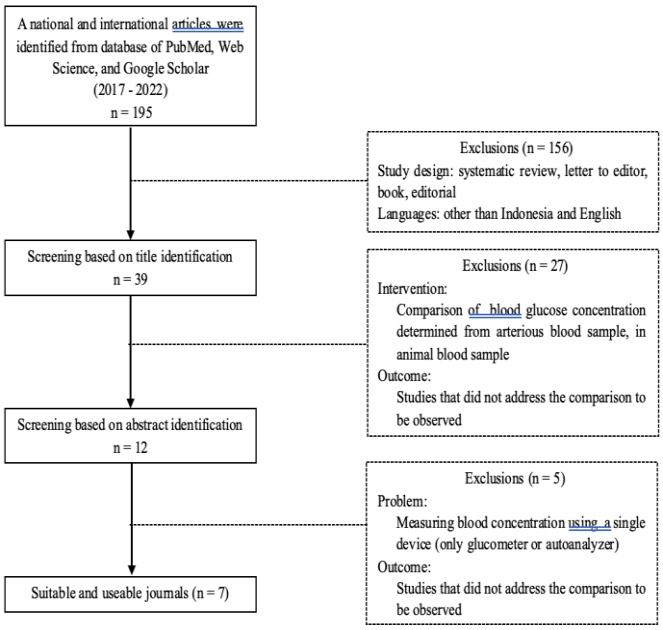

Fig. 1: Flow diagram of the search and selection articles process

III. RESULTS

The results of the data search, identified 195 relevant studies through the database that was previously mentioned using keywords and filters. A 156 full text articles excluded after the study design and language analysis, then 27 articles excluded after the title and analysis analysis, therefore 12 articles assess for eligility. In the final stage of the eligibility assessment, 5 articles were excluded and the remaining 7 studies were included in this review.

Table 2: Summary of the main characteristics of the selected studies

No.	Category	N	%
A.	**Publication year**		
	2017	3	43
	2018	3	43
	2020	1	14
		7	**100**
B.	**Language**		
	Indonesia	0	0
	English	7	100
		7	**100**
C.	**Database**		
	Pubmed	0	0
	Google Scholar	1	14
	Web of Science	6	86
		7	**100**

D.	**Statistical Analysis**		
	Cross sectional	7	100
		7	**100**
E.	**Sampling method**		
	Random	2	28
	Purposive	5	72
		7	**100**
F.	**Data Analysis**		
	Independent t test	1	14
	Pearson's correlation	4	58
	Paired t test	1	14
	Regression analysis	1	14
		7	**100**

The selected studies were published in English, within a 5 years (2017 - 2022). All design study was a cross sectional studies, both descriptive cross sectional studies and analytical cross sectional studies. Purposive sampling and random sampling used to obtain the participant (samples). Most of the studies analysis determined by Pearson correlation.

Table 3: A total 7 selected studies

No.	Author	Year	Journal, Volume	Title	Method (Design, Sample, Variabel, Instrument, Analysis)	Result	Database
1.	Kanwugu O N, *et.al.*,[9]	2017	BMC Res Notes 10:53	A comparative assessment of the glucose monitor (SD Codefree) and auto analyzer (BT-3000) in measuring blood glucose concentration among diabetic patients	D: Cross sectional study S: Random sampling V: Blood glucose concentration determined from venous and capillary blood glucose from diabetic and non-diabetic patients I: Glucometer and Autoanalyzer A: Independent t test	The mean glucose concentration for the diabetic patients (n = 100) using the glucometer were not significantly different from that of the auto analyser (10.16 ± 3.708 mmol/L vs. 9.458 ± 3.204 mmol/L, p = 0.154), though the glucometer generally overestimated the glucose concentration.	Web of Science
2.	Selvakumar P, Vivek G[10]	2017	International Journal of Pediatric Research Vol 4/ Issue 07	Blood glucose measurement by glucometer in comparison with standard method in the diagnosis of hypoglycemia in sick neonates	D: Cross sectional study S: Purposive sampling V: Correlation of capillary and venous bedside glucose estimation in sick hypoglycemic neonates. I: Glucometer and Autoanalyzer A: Pearson's correlation	The correlation coefficient for the lab blood glucose versus the capillary blood glucometer glucose was 0.919 and the correlation coefficient for the laboratory glucose (blood glucose level > 40mg%) and venous glucometer glucose was 0.928 in sick neonates. The correlation coefficient for the lab blood glucose versus the capillary blood glucometer glucose was 0.237 and the correlation coefficient for the laboratory glucose and venous glucometer glucose was 0.216 (blood glucose level < 40mg%)	Web of Science
3.	Mallick AK, Ahsan M[11]	2017	International Journal of Clinical Biochemistry and Research; 4(3):220-224	A comparative study of glucose concentration determined from venous plasma sample and capillary blood sample	D: Cross sectional study S: Random sampling V: Blood glucose concentration (<60mg/dL, 61-299 mg/dL, >300mg/dL) determined from venous and capillary blood glucose I: Glucometer and Autoanalyzer A: Paired t test	Glucose levels determined by a glucometer and GOD-POD method showed very good correlation (r=0.958;*p<0.001*) However, at very high and low glucose levels, the glucometer significantly under estimated (*p=0.014*) and over-estimated (*p<0.001*) the glucose levels respectively	Web of Science
4.	Mitra S., Kumar Prashant, and Dey Madhusudan[12]	2018	Medical Science; 7(2):342-6	A comparative study between capillary and venous blood glucose levels of type 2 diabetes mellitus patients	D: Descriptive Cross Sectional Study (descriptive analysis) S: Purposive sampling V: Blood glucose concentration determined from venous and capillary blood glucose of DMT2 patient in ICU	A good correlation between the CBG and VBG of sample 1 (R^2 = 0.995, p<0.05), sample 2 (R^2 = 0.986, p<0.05) and sample 3 (R^2 = 0.988, p<0.05). Similarly a good correlation also existed between CBG and VBG at <250 mg /dl and > 250mg/dl which	Google scholar

				in the intensive care units	I: Glucometer and Autoanalyzer ERBA A: Pearson's correlation	was (R^2 = 0.943, p<0.05) and (R^2= 0.989, p<0.05) respectively	
5.	Topcuoglu C, Yilmaz FM, Kaya O, Cakir B[13]	2018	Medicine Science Med Science;7 (1):218-21	Verification studies in glucometers: Should we use capillary blood or venous blood for comparison?	D: Cross sectional study S: Purposive sampling V: Comparing the results of the glucose in fasting dan postprandial from capillary and venous blood samples I: Glucometer and Autoanalyzer A: Regression analysis	Regression analysis: • Fasting state y = 0,873x + 24,32 (r = 0,857) equation between Accu-chek and venous blood glucose y = 0,9x + 16,15 (r = 0,920) equation between Accu-chek and capillary blood glucose y = 0,811x + 2094 (r = 0,776) equation between GlucoMax venous blood glucose, y = 0,851x + 12,28 (r = 0,863) equation with GlucoMax capillary blood glucose • Postprandial state y = 0,713x + 48,46 (r = 0,258) equation between Accu-chek and venous blood glucose y = 0,981x + 11,77 (r = 0,718) equation with capillary blood glucose y = 0,706x + 39,12 (r = 0,453) equation between GlucoMax and venous blood glucose, y = 0,790 + 22,35 (r = 0,787) equation between GlucoMax capillary blood glucose	Web of Science
6.	Baygutalp NK, Bakan E, Bayraktutan Z, and Umudum FZ[14]	2018	Turk J Biochem; 43(5): 510–519	The comparison of two glucose measurement systems: POCT devices versus central laboratory	D: Descriptive Cross Sectional Study (descriptive analysis) S: Purposive sampling V: Determine the test reliability of glucose meters and to compare their results with those of the clinical laboratory method. I: Glucometer and Autoanalyzer A: Pearson's correlation and Spearman's correlation test for each glucometer. The results of the two analyzers, GMS and laboratory analyzer, were compared using Passing-Bablok and Bland-Altman plots for association and differences.	Significant correlations were found for all GMS – laboratory comparison [for all GLU, for GLU ≤100, and GLU >100; r = 0.955, 0.545, 0.958, respectively]. On the Passing – Bablok Regression analysis, all the regressions associated with GLU concentrations >100 mg/dL showed good concordance between GMSs and the laboratory method. Conversely, lower correlation or poor concordance or the measurement of GLU concentrations <100 mg. Bland-Altman plots showing the compatibility between GMSs and laboratory measurements	Web of Science
7.	Sirohi R, Ravi Pratap Sing RP, Chauhan K[15]	2020	Indian Journal of Public Health Research & Development, July 2020, Vol. 11, No. 7	A comparative study of Venous and Capillary blood glucose in a Tertiary Care Hospital	D: Analytival Cross sectional study (Comparison study) S: Purposive sampling V: Determine the mean difference and correlation between capillary and laboratory venous plasma glucose estimation in fasting state of diabetic and control group I: Glucometer and Autoanalyzer A: Pearson's correlation	A good correlation between capillary and venous plasma glucose level in all the subjects (R^2 = 0,991), control group (R^2 = 0,851) and diabetic group (R^2 = 0,994). It was observed that there was a significant difference between capillary and venous blood glucose values. The capillary blood glucose value on an average was 10.19% higher than venous blood glucose values.	Web of Science

Kanwugu O N, *et.al*., (2017) was conducted a cross sectional study to determine how well the measurements from a glucometer (SD Codefree) from a standard auto analyser (BT-3000) using blood samples from diabetic and non-diabetic patients at the Bolgatanga Regional Hospital in Ghana. A total of 150 randomly selected patients; 100 diabetic patients (4 type 1 and 96 type II) and 50 non diabetic patients. Venous blood sample were obtained from ante-cubital venous and capillary blood sample were obtained from after the patients following standard procedures, and blood glucose concentrations were determined using the two methods respectively. The comparison of the mean values from the two methods was done using independent t test at a 95% confidence interval and the differences were considered statistically significant if $p < 0.05$. All the results indicated a good and significant correlation between the glucometer and the auto

analyzer (Pearson correlation coefficient, $R^2 = 0.862$, $p < 0.001$). Kanwugu O N, *et.al*. resume that the glucometer (SD Codefree) is as accurate as the auto analyser and therefore can be conveniently used as a rapid easy-to-use alternative.[9]

The efficacy and correlation of capillary and venous glucose concentration by glucometer (Accu check active) in comparison with laboratory blood glucose concnetration by glucose oxidase method in sick neonates studied by Selvakumar P and Vivek G (2017). Of the 200 neonate s screened, 31 were hypoglycemic (blood glucose concentration < 40mg/dl), 164 neonates (blood glucose concentration 40 – 150mg/dl), and 5 neonates (blood glucose concentration > 150 mg/dl). The Pearson corellation coefficient for the lab blood glucose versus the capillary blood glucometer glucose was 0.919 and the Pearson correlation coefficient for the laboratory glucose and venous glucometer glucose was 0.928 in sick neonates (in group neonatus blood glucose > 40mg/dl). When the laboratory blood glucose was < 40mg/dl, the Pearson correlation coefficient for the lab blood glucose versus the capillary blood glucometer glucose was 0.237 and the Pearson correlation coefficient for the laboratory glucose and venous glucometer glucose was 0.216.[10]

A comparative study of blood glucose concentration determined from venous plasma sample and capillary blood sample was conducted by Mallick AK and Ahsan M in 2017. This study was carried out on the patients attending the OPD, camps and those admitted in the ICU and casualty at Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh. Two hundred patients were randomly selected for the study, their venous blood samples were determined by GOD-POD test. Simultaneously their capillary blood glucose were also determined by a glucometer. Statistical analysis using paired t test results that blood glucose concentration determined by a glucometer and GOD-POD method showed very good correlation ($r = 0.958$; $p < 0.001$). However, at very high and low blood glucose concentration, the glucometer significantly under estimated ($p = 0.014$) and over-estimated ($p < 0.001$) the blood glucose concentration respectively.[11]

Another comparative study to determine the correlation of capillary blood glucose versus venous blood glucose was conducted in a large tertiary care hospital, Pune, India. This study was a cross sectional, descriptive study, 65 patients hyperglycemic type 2 diabetes mellitus patients admitted in ICU were included in this study. The laboratory results and glucose strip results were tabulated as sample 1 (capillary/venous- time of admission), sample 2 (capillary /venous – 24 hrs), sample 3 (capillary /venous – 48 hrs) and also segregated into less than 250 mg/dl and more than 250 mg/dl for determining the correlation and agreement between the capillary and venous blood glucose concentration. A good correlation between the CBG and VBG of sample 1 ($R^2 = 0.995$, $p<0.05$), sample 2 ($R^2 = 0.986$, $p<0.05$) and sample 3 ($R^2 = 0.988$, $p<0.05$). Similarly a good correlation also existed between CBG and VBG at <250 mg /dl and > 250mg/dl which was ($R^2 = 0.943$, $p<0.05$) and ($R^2= 0.989$, $p<0.05$) respectively. Mitra S., Kumar Prashant, and Dey Madhusudan concluded that in T2DM patients admitted in ICU we should use finger prick method using glucometer to measure blood glucose levels, if all the confounding factors which impede with the measurement of blood glucose are taken into consideration.[12]

Topcuoglu C, Yilmaz FM, Kaya O, and Cakir B (2018) were conducted a study in Ankara, Turkey, aimed to compare two different glucometer glucose results with the venous and capillary blood glucose results measured in routine biochemical analyzers. Of 101 samples taken from volunteer subjects, 81 were taken in fasting state, and 20 were taken in postprandial state. In the fasting and postprandial state, the capillary glucose levels showed better correlation with glucometer measurements than venous blood glucose levels.[13]

Baygutalp NK, Bakan E, Bayraktutan Z, and Umudum FZ were studied the the comparison of two glucose measurement system POCT devices versus central laboratory. This study was conducted in Clinical Biochemistry Laboratory of Ataturk University Research Hospital by using the blood samples taken from hospitalized patients. Of 1837 glucose meters read-outs, 1748 capillary and venous comparisons were evaluated. Pearson's correlation and Spearman's correlation test for each glucometer. The results of the two analyzers, GMS and laboratory analyzer, were compared using Passing-Bablok and Bland-Altman plots for association and differences. Significant correlations were found for all GMS – laboratory comparison (for all GLU, for GLU ≤100, and GLU >100; r = 0.955, 0.545, 0.958, respectively). On the Passing – Bablok Regression analysis, all the regressions associated with GLU concentrations >100 mg/dL showed good concordance between GMSs and the laboratory method. Conversely, lower correlation or poor concordance or the measurement of GLU concentrations <100 mg. Bland-Altman plots showing the compatibility between GMSs and laboratory measurements.[14]

A comparative study of Venous and Capillary blood glucose in a Tertiary Care Hospital, Meerut, India was conducted by Sirohi R, Ravi Pratap Sing RP, Chauhan K. Total 373 subjects (176 males and 197 females) including 149 cases with altered glucose levels and 224 control subjects were studied. After overnight fasting, capillary blood glucose by glucometer and venous plasma glucose by Siemens autoanalyzer were estimated from all subjects, aged above 18 years. Both samples were taken at the same time. Mean difference and correlation coefficient were determined. A good correlation between capillary

and venous plasma glucose level in all the subjects (R2 = 0,991), control group (R2 = 0,851) and diabetic group (R2 = 0,994). It was observed that there was a significant difference between capillary and venous blood glucose values. The capillary blood glucose value on an average was 10.19% higher than venous blood glucose values. It was concluded that glucometer, as a sole measuring device in a hospital setup, is not satisfactory. The venous blood glucose is a better indicator and is of utmost importance for confirmatory results.[15]

IV. DISCUSSION

Glucose is the major carbohydrate found in the blood and a source of energy in human body. The nervous system totally depends on glucose from the surrounding extra cellular fluid (ECF) for energy, so the concentration of glucose in the ECF must be maintained. When the concentration falls below a critical level, the nervous tissues lose the primary energy source and are incapable of maintaining normal function. Several factors can affect blood glucose levels, including: lack of exercise, increased food intake, increased physical stress and emotion, increased age and weight, the influence of steroids and other drugs.[16]

The report from Basic Health Research (Riskesdas) in 2018 shows that the prevalence of diabetes mellitus in Indonesia for all ages is 1.5%. Many people with diabetes are required to regularly check their current blood glucose concentrations.[17] With advancing technology to improved patient management, the use of point of care test (POCT) equipment such as glucometers (are small handheld devices that can be used to measure capillary blood glucose using just a drop of blood) has gained increasing popularity. It has become obvious that the efficient use of glucometers in the clinical and private setting is essential for the effective management of all types of diabetes mellitus. Glucometers are used in the clinics and wards routinely as a form of support for the laboratory.[18,19]

In this systematic review, the authors reviewed 7 research articles about blood glucose concentration determined from venous and capillary blood glucose. The result of this review were have the same results, a good correlation between venous and capillary blood glucose. Kanwugu O N, *et.al*. was resumed that the glucometer is as accurate as the laboratory method and therefore can be conveniently used as a rapid easy to use alternative.[9] A good correlation between venous and capillary blood glucose was observed by Selvakumar P and Vivek G (2017). Venous and capillary blood glucose examination by glucometer has a good sensitivity and negative predictive value in detecting hypoglycemia in sick neonates. The sensitivity of glucometer using venous blood is superior to capillary sample estimates. Selvakumar P and Vivek G suggest laboratory method should still be performed if glucometers reading are in the hypoglycemic range.[10] A comparative studies were conducted by Mallick AK and Ahsan M in Uttar Pradesh 2017, Mitra S., Kumar Prashant, and Dey Madhusudan in Pune, India 2018, Topcuoglu C, Yilmaz FM, Kaya O, and Cakir B in Ankara, Turkey 2018, Baygutalp NK, Bakan E, Bayraktutan Z, and Umudum FZ in Ataturk, Turkey 2018. A good correlation has been observed between venous and capillary blood glucose. The authors resumed although glucometers are useful for self-monitoring and keeping records of glycemic control, they should be used with caution in emergency hypoglycemic and hyperglycemia condition. In these condition it is advisable to determine and confirm the glucose concentration in the laboratory.[11,12,13,14] Slightly different with a comparative study of venous and capillary blood glucose was conducted by Sirohi R, Ravi Pratap Sing RP, Chauhan K. They were concluded a good correlation between venous and capillary blood glucose level in all the subjects but they also observed that there was a significant difference between venous and blood glucose values. The capillary blood glucose value on an average was 10.19% higher than venous blood glucose values.[15]

Blood glucose concentration in the capillary differ from those in the veins. Venous plasma glucose concentration is the estimated glucose after utilization of glucose by tissues. It depends on the extent of tissue extraction of glucose and the effect of insulin and insulin counterregulatory hormones. Plasma generally has more liquid content than whole blood and tends to give a slightly higher glucose value than whole blood.[11]

The accuracy of blood glucose concentration results with a glucometer is adjusted to namely pre analytic, analytic and post analytic stage. An error in the pre-analytic stage can contribute around 61%, while the error in the analytic stage is 25% and an error in the post-analytic stage is 14%. The pre-analytic stage is the stage of determining the quality of the sample to be used in the examination. The pre-analytic stage that is often carried out by the laboratory is taking capillary blood. Capillary blood draw or skin punture is usually performed is at the edge of the tip of the middle or ring finger also heel area for certain examinations that require a small amount of blood.[20]

The limitation of this study was the variation of glucometer and laboratory method to measure the blood glucose concentration. The difference in blood glucose concentration by the glucometers and the standard laboratory method may be differ by many factors from pra analytical, analytical, and post analytical stage.

V. CONCLUSION AND SUGGESTIONS

A. Conclusion

In this systematic review, the authors reviewed 7 research articles about blood glucose concentration determined from venous and capillary blood glucose. The result of this review were have the same results, a good correlation between venous and capillary blood glucose. Caution must be exercised in accepting the results of glucometers using as substitutes for a laboratory blood glucose result. Clinicians should always correlate the blood glucose reading with the clinical findings in taking their management decisions.

B. Suggestion

For future researchers, it is hoped that the results of this literature review will be data resources and research references related to compare blood glucose concentration determined from venous blood and capillary blood and and other blood samples.

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