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Short Communication

Innovative utilization of menstrual blood for determination of HbA1c, FSH, LH, AMH cholesterol,CRP quantitiesin infertile women with no access to medical facilities/cost factor/fear of pricks for facilitating early access for assisted reproductive technology(ART)-advantages of simultaneous testing of ones needing blood/serum- A Short Communication

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Abstract

Recently,Nasseri et al. have been pursuing the determination of HbA1c FSH, LH, AMH cholesterol,CRP quantities in infertile -advantages of simultaneous testing of ones needing blood/serum- quantities,.They generated a specific kind of pad alias Q pad having unsaturated strips for the determination of the serum markers.These pads are requiredto be applied for a minimum of 4 hrs for the unsaturated strips to pick up the quantities.This is particularly of use for women seeking infertility treatment with , no access .Furtherthere observations were that these pads were good enough for determination of some steroid hormones normally evaluated in serum while HbA1c from venous blood both and in there multiple asssessments they found concordance of HbA1cand these hormones.The only disadvantage was with menstrual cycle having lesser quantities at that time for instance estradiol(E2) quantitiewhich might fall below the minimalaccepted limits of the range of test Otherwise it might be of cons use in infertile women with no access to medical facilities/cost factor/fear of pricks for facilitating early access for assisted reproductive technology(ART)once they have their day 2 values assessed besides even in invitro fertilization(IVF) lesser pricks needed .This needs to be further pursued as even in women with Polycystic ovary women syndrome (PCOS) one can perform other tests needed further.

Key Words-Menstrual effluent; HbA1c ;FSH;LH; AMH; cholesterol;CRPtesting

Introduction

Routine blood evaluation monitors metabolic markers for instance hemoglobin A1c (HbA1c), thyroid hormones, as well as a variation of necessary nutrients to aid in isolating early signs of disease risk, prescribing preventive care, as well as follow the manner treatments affected systemic health. Pertaining to the women's reproductive healthcare, clinicians determine blood quantities of crucial hormones correlated with fertility when screening for disorders for instance polycystic ovary syndrome(PCOS), ovarian insufficiency(POI), along with thyroid disorders (1, 2). Intrapopulation variation in serum hormone quantities are impacted by

various factors, inclusive off age, caloric consumption, in addition to physical activity quantities (3). Standard practice for hormone determination depends on blood specimens acquired via venipuncture, an approach having requirement for assistance from medical personnel along with might result in physical as well as emotional discomfort for the patient. Venipuncture methodologies stimulate physiological stress reactions correlated with the prediction of pain, despite repeated exposures (4). Despite at-home testing possess the capacity of escalating healthcare accessibility, the acquisition of venipuncture blood samples at home usually needs particular processing, storage, in addition to temperature- regulated, speeded up transportation (5).Akin storage along with transport restrictions influence reproductive hormone asssessment in noninvasive alternative samples, for instance saliva in addition to urine (3). Sequentially, women usually encounter significant hurdles in receiving fertility specialist consultations as well as reproductive hormone asssessment, emphasizing the need for expanding accessibility to these tests (6). Recently, fingerstick sampling via dried blood spot (DBS) has been asssessed in the form of a more convenient along with cheaper alternative to a venous blood draw for controlling of HbA1c in addition to hormone quantities (7). Dried blood spot sampling conserves blood samples, enabling patients to self-collect specimens without needing to travel to a doctor's office (5, 8). Blood is collected on filter paper, followed by the drying of the samples which are shipped to a clinical laboratory for asssessment. Nevertheless, despite fingerstick blood sampling with DBS takes care of certain of the logistical hurdles correlated with venipuncture, plethora of individuals are still not comfortable with the self delivery of a fingerstick test in view of the plausible pain as well as soreness. Asssessment of physiological along with psychological stress reactions poses a hurdle regarding the properties of fingerstick in the form of essentially ''less invasive'' in contrast to venipuncture, since participants' stress reactions to fingerstick were akin to (as well as for certain measures greater than) their reaction to venipuncture (9). Conversely, venipuncture or fingerstick estimation by blood sampling, menstrual effluent presents a fully noninvasive, passively collected biological sample for biomarker monitoring. Menstrual effluent comprises of whole blood, vaginal fluids, as well as tissues shed from the endometrial lining in reaction to hormonal signaling (10). Although its possesses a complicated constitution along with proinflammatory molecular signature (11, 12), recent studies have revealed an intricate association amongst menstrual as well as peripheral blood for inflammatory biomarkers (13),

Recently, Nasseri et al.[14], published an article entitled'' Concordance of haemoglobin A1c (HbA1c) and reproductive hormone levels in menstrual and venous blood', where they revealed the approach of utilization of menstrual effluent along with a dried blood spot(DBS) in a particularly designed pad- the Q

pad-possessing unsaturated stripsn for the determination(whichcheckedeon 3-4 h of use) of the serum markers with the utilization of standard laboratory methodologies in addition to non invasive approaches .This methodology was first displayed in 1989[15], as well as subsequentlyit has been an attractive ;albeit minimally used for accumulating significant knowledge in reference to ovarian working. Menstrual effluent gets constituted of whole blood as well as vaginal fluids in addition to endometrial tissues[16], along with the Q pad might be utilized for the estimation of both the markers where whole blood is the requirement for instance HbA1c quantities as well as the ones requiring serum for instance follicle stimulating hormone (FSH), Luteinizing hormone(LH) in addition to antimullerian hormone (AMH) quantities along with other steroid hormone quantities. Earlier studies had illustrated a greater association amongst menstrual blood as well as peripheral blood determination of HbA1c[17] quantities, FSH quantities, lipoprotein quantities in addition to quantities of other markers[1] as well as cholesterol, in addition to high-sensitivity C-reactive protein[18]. The association amongst menstrual DBS evaluation along with serum in this particular study is good as well as the researchers have paid attention with reference to asssessment of the actions of the different vaginal contaminations in the form of the actions of the semen, vaginal medicines,urine in addition to others with just the contamination with faeces having an effect. Despite,this is not any innovative strategy along with other studies have performed the asssessment of its applicability,this portrays the advantages of being a prospective controlled study of significance.

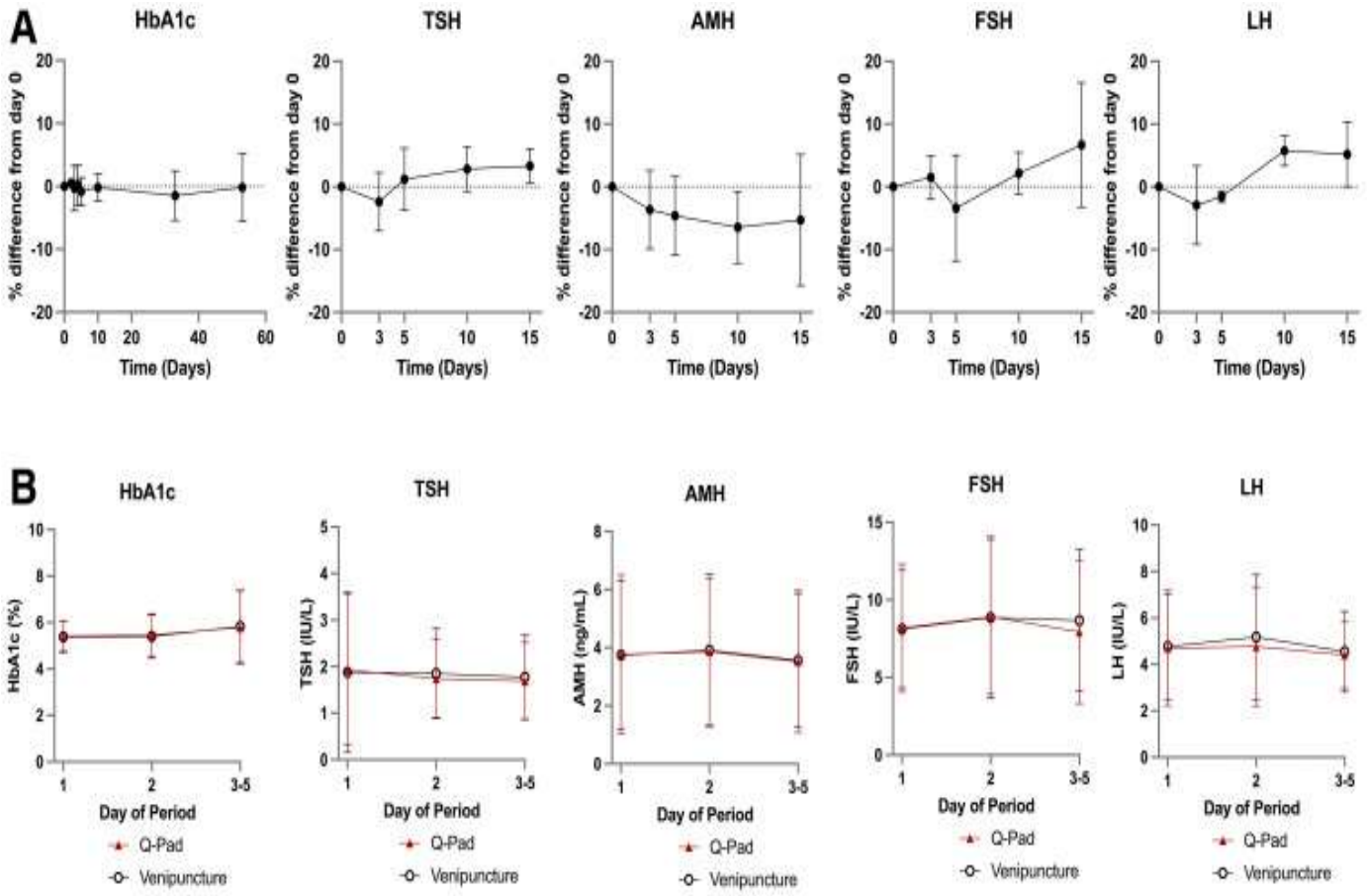

Figure 1: Courtesyref no-14-Stability of menstrual dried blood spot (DBS) samples was assayed by testing Q-Pad samples from three participants over a time course of 0–53 days for hemoglobin A1c (HbA1c) analysis and 0–15 days for hormone analysis. Graphs depict the percent difference from the DBS sample measurement on day 0. (B) Mean HbA1c and hormone levels in Q-Pad and matching venipuncture samples were compared for participants who collected menstrual samples on days 1, 2, or 3–5 of their period. Data are presented as the mean ± SD. Differences between timepoints were not significant (two-way ANOVA, *P*>.05). AMH = anti-müllerian hormone; HbA1c = hemoglobin A1c; FSH = follicle-stimulating hormone; LH = luteinizing hormone; TSH = thyroid stimulating hormone.

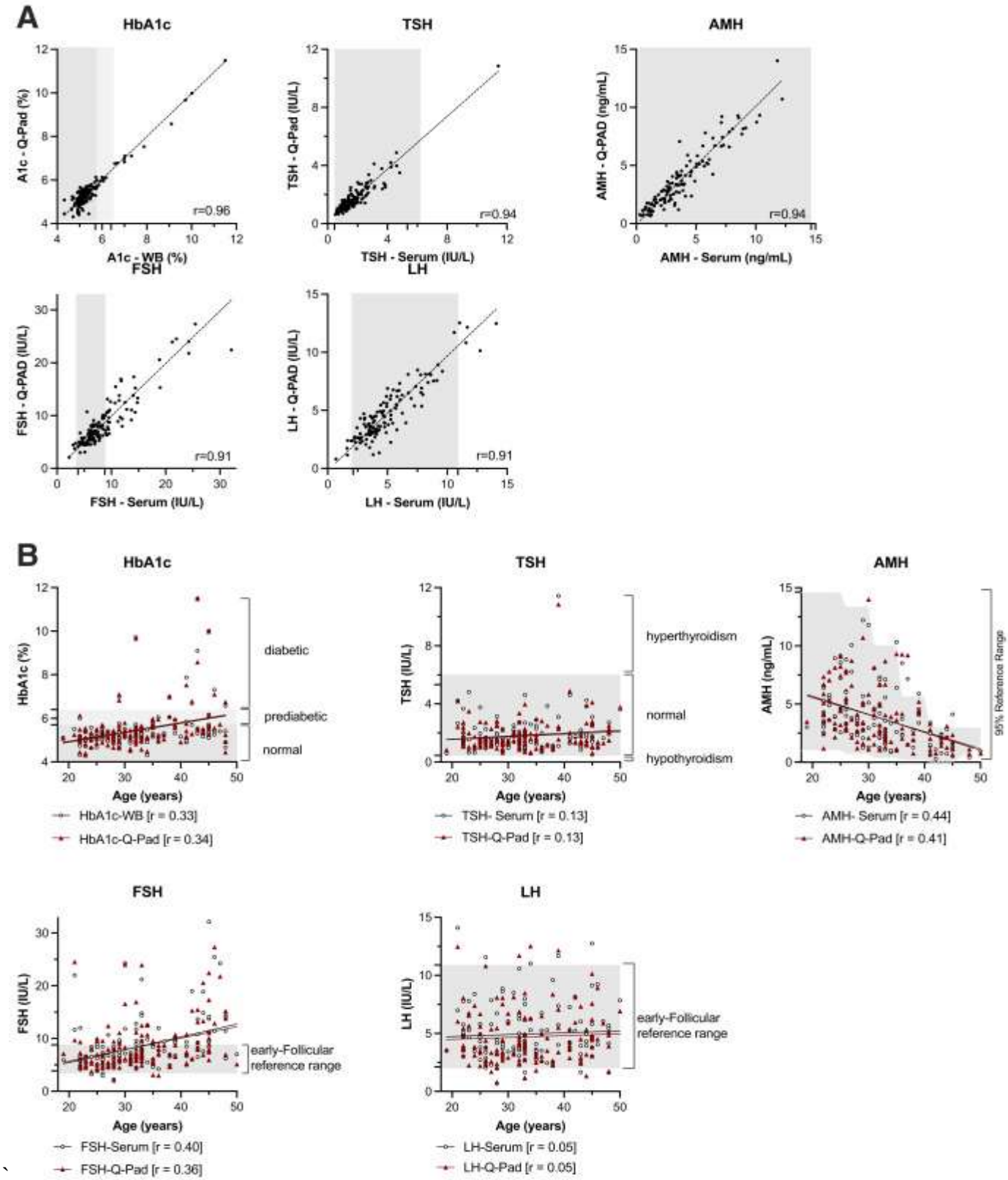

Figure 2: Courtesyref no-14- **(A**) Deming linear regression for analyte measurements in menstrual blood (Q-

Pad sample) vs. conventional blood draw. The gray region indicates the reference range of the analyte for healthy populations aged 18–45 years. Follicle-stimulating hormone (FSH) and LH reference ranges provided for early-follicular phase. (**B**) Pearson linear correlation for Q-Pad and venipuncture samples vs. subject age. The gray region indicates the reference ranges for healthy populations. AMH = anti-müllerian hormone; HbA1c = hemoglobin A1c; FSH = follicle-stimulating hormone; LH = luteinizing hormone; TSH = thyroid stimulating hormone; WB = whole blood.

The capacity of the patients in collecting the specimen is of benefit at their own house in case of transportation to the laboratory was not feasible in view of no accessibility along with availability for treatment was complex. Additionally, no stress encountered in collecting the specimen would escalate the probability of compliance doing the same for the patients for instance adolescents,ii) the ones having fear for the needle pricks iii)or full women categorized unsuitable for venipuncture . Nevertheless non invasive approaches continued to be promising subsequent to over 30yrs of work. The explaination offered was the reduction of precision of the markers having lesser quantities at the time of menstrual cycle for instance estradiol(E2) quantities.

However,this methodology would be having requirement for evaluation in the real world population .This study displayed approximately 25%of patients who gave consent failed to finish their taking part prior to attaining the samples, which has been revealed to be in the form of restriction of this study .Of greater significance was that of the samples estimated ,11-20%did not yield any outcomes in view of problems encountered for instance unsaturated strips, contamination with faeces,or at the time of collecting serum sample there were reduction in the values much lesser in contrast to test range.As per Nasseri et al.[1],this occurred from patients problems.Asper their views requirement for taking into account sufficient proper directions accompanied by correction of medical lapses.This extra botheration for the practitioners would need assessment.

In view of maximum women going through evaluation for infertility, the earlier assessment is inclusive of determination of FSH, LH, AMH, in addition to E2quantities usuallyon the day 2-4 of the menstrual cycle, therefore the estimation of these markers in the menstrual effluent might work ideally. Addition of AMH would aid in fulfilling the total assessment of the ovarian reserve.This non invasive approach looks attractive;

since it aids in evaluating large chunk of women regarding their plausibility for fertility once seeking conception giving reproductive freedom. On requirement for greater assessment these might be pacily achieved by the reproductive endocrinologists for taking precise decision.

Conclusions

This investigational modality would escalate the accessibility of care provision to underprivileged women / from lesser socioeconomic strata, difficulty in obtaining transportation, care for children or laboratory having phlebotomy facilities placed distantly in addition to this would be particularly advantageous for the initiatial asssessment of ovarian reserve. Furthermore ,it might be aiding in amelioration of minimum of venipunctures at the time of invitro fertilization(IVF) treatment cycles.

This kind of methodology needs to be encouraged in reference to generation for the improvement of quality of life (QOL) of these women considerably[19].

References

1. Wheeler MJ.The measurement of LH, FSH, and prolactin. Methods Mol Biol 2013;1065:105-16.

2. Broer SL, Broekmans FJ, Laven JS, Fauser BC. Anti-Mullerian hormone: ovarian reserve testing and its potential clinical implications. Hum Reprod Update 2014;20:688–701.

3. Gildner TE. Reproductive hormone measurement from minimally invasive sample types: methodological considerations and anthropological importance. Am J Hum Biol 2021;33:e23535. 4.

4. Weckesser LJ, Plessow F, Pilhatsch M, Muehlhan M, Kirschbaum C, Miller R. Do venepuncture procedures induce cortisol responses? A review, study, and synthesis for stress research [study]. Psychoneuroendocrinology 2014; 46:88–99.

5. Freeman JD, Rosman LM, Ratcliff JD, Strickland PT, Graham DR, Silbergeld EK. State of the science in dried blood spots. Clin Chem 2018; 64:656–79.

6. Worthington AK, Burke EE, Shirazi TN, Leahy C. US women's perceptions and acceptance of new reproductive health technologies. Womens Health Rep 2020;1:402–12.

7. Burke EE, Beqaj S, Douglas NC, Luo R. Concordance of fingerstick and venipuncture sampling for fertility hormones. Obstet Gynecol 2019;133:343–8.

8. McDade TW, Woodruff TK, Huang YY, Funk WE, Prewitt M, Kondapalli L, et al. Quantification of anti-Mullerian hormone (AMH) in dried blood spots: € validation of a minimally invasive method for assessing ovarian reserve. Hum Reprod 2012;27:2503–8.

9. Lorenz TK. Autonomic, endocrine, and psychological stress responses to different forms of blood draw. PLOS ONE 2021;16:e0257110.

10. Yang H, Zhou B, Prinz M, Siegel D. Proteomic analysis of menstrual blood. Mol Cell Proteomics 2012;11:1024–35.

11. Crona Guterstam Y, Strunz B, Ivarsson MA, Zimmer C, Melin AS, Jonasson AF, et al. The cytokine profile of menstrual blood. Acta Obstet Gynecol Scand 2021;100:339–46.

12. Naseri S, Rosenberg-Hasson Y, Maecker HT, Avrutsky MI, Blumenthal PD. A cross-sectional study comparing the inflammatory profile of menstrual effluent vs. peripheral blood. Health Sci Rep 2023;6:e1038.

13. da Silva CM, Vilac¸a Belo A, Passos Andrade S, Peixoto Campos P, Cristina Franc¸a Ferreira M, Lopes da Silva-Filho A, et al. Identification of local angiogenic and inflammatory markers in the menstrual blood of women with endometriosis. Biomed Pharmacother 2014;68:899–904.

14. Nasseri S,Avrutsky M,Capati C,Desai D,A R Blumenthal P. Concordance of haemoglobin A1c (HbA1c) and reproductive hormone levels in menstrual andvenous blood.FS Rep2024;5:33-9.

15. ZhouJP, Fraser JS,Caterson I, Grivas A,McCarson G,Norman D,etal. reproductive hormones in menstrual blood. J Clin Endocrinol Metab 2007;92(8):3068-75.

16. YangH, ZhouB,PrinzM,SiegelD. proteomic -analysis of menstrual blood. Mol CellProteomics 2012; 11: 1024-35.

17. Nasseri S,Brewster RCL, Blumenthal P.Novel use of menstrual blood for monitoring theglycaemic control in patients with diabetes:proof of concept study. BMJSex Reprod Health 2022;48:123-7.

18. Naseri S, Lerma K, Blumenthal P. Comparative assessment of serum versus menstrual blood for diagnostic purposes: a pilot study. J Clin Lab Med 2019;4.

19. Detti L,Gibbson WE. Hormonal testing in menstrual blood enhances reproductive freedom. FS Rep2024;5:13-13.

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