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Comparison of The Accuracy of Bacteria Urinalysis and Vaginal Swab (Culture) as The Screening Test to Predict Preterm Birth

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Abstract Preterm birth refers to the birth of a baby before the developing organs are mature enough to allow normal postnatal survival. Thus, premature infants are at greater risk for short and long term complications, including disabilities and impediments in growth and mental development. This research is conducted as part of the prevention efforts in the terms of early screening for preterm births. This research is aimed at comparing the accuracy between bacteriuria analysis and vaginal swab (culture) to predict a preterm birth outcome. This research is a prospective observational study with high similarity with diagnostic test in the exception that this study uses the occurrence of preterm birth itself as the so-called gold standard. Mothers who visit Puskesmas (Community Health Centre) and District Hospital for antenatal care or delivery Yogyakarta, Indonesia are recruited and taken urine and vaginal swab sample.Bacteria urinalysis has sensitivity 36.1%, specificity 33.8%, positive predictive value (PPV) 22.4% and negative predictive value (NPV) 50%. Vaginal swab culture in predicting for preterm birth has sensitivity of 47.2%, specificity of 80.8%, positive predictive value 56.6% and negative predictive value of 74.3%.Urinalysis has not been proven to be useful in predicting preterm birth. In the other hand, vaginal swab culture can be useful in ruling out preterm birth occurrences especially in high-risk pregnant women.

Keywords: preterm birth; bacteria urinalysis; vaginal swab culture.

1. Introduction

Preterm birth refers to the birth of a baby before the developing organs are mature enough to allow normal postnatal survival. Thus, premature infants are at greater risk for short and long term complications, including disabilities and impediments in growth and mental development[1]. It is said that preterm birth is the most common cause of neonatal death[2]. It is associated with 75% of perinatal morbidity and mortality for infants born without congenital anomalies[3].

Due to its short and long term complications, preterm birth has been a significant burden for the family and also the nation, economically and socially. It is reported that the United States spends approximately 5 billion dollars – which is around 50 trillion rupiahs - to deal with their number of preterm births, which is actually less in numbers than the developing countries, including Indonesia[4].

Whilst significant progress has been made in the care of premature infants, very little stresses in reducing the prevalence of preterm birth[1]. Whereas we know that if we are able to prevent the occurrence of preterm birth means we can reduce the number of neonatal death.

Establishing a prediction tool is one of the prevention efforts we are able to perform which enables the health providers and also the mother and her family to take initial action thus resulting in better outcome and increase the survival rate of the infants. In the long run, besides that it will ease the burden of the family, it will also ease the nation's burden in this particular issue.

Therefore, this research is conducted as part of the prevention efforts in the terms of providing such prediction tool for preterm births.

The major existing predicting tool for preterm birth consists of cervical length measurement, fibronectin testing, uterine contraction monitoring and biomarkers detection. With details of its measurements as follows,

Tabel 1: Prediction at 22–24 Weeks of Spontaneous Preterm Birth Before 35 Weeks' Gestation[5]

Prediction tool	Sensitivity (%)	Specificity (%)	Predictive value	
			Positive (%)	Negative (%)
Uterine contraction	6.7	92.3	25.0	84.7
Cervical length measurement	40.8	89.5	42.6	88.8
Fibronectin	18.0	95.3	42.9	85.6

As for biomarkers, it depends on what kind of substance is the focus. There are at least 22 biomarkers that have been explored, where none meet the criteria to be considered a clinically useful test to predict spontaneous preterm birth.

Infection is thought to be the cause of up to 40% of cases of preterm birth, including many 'idiopathic' or unexplained cases. Figure 1 is a implified model of the pathophysiology of infection-induced preterm labor triggered by activation of the maternal and fetal innate immune systems. The proposed signaling cascade likely involves a high degree of positive and negative feedback looping, multiple redundant pathways, and interaction between the maternal and fetal compartments (depicted schematically in the figure by arrows; however it should be noted that these interactions occur in several directions and on several levels simultaneously). NFκB, nuclear factor κB; AP-1, activator protein 1; STAT, signal transducers and activators of transcription; IRF, interferon regulatory factor; TNF, tumor necrosis factor; IL, interleukin; MIP, macrophage inflammatory protein; MCP, macrophage/monocyte chemo-attractant protein[6].

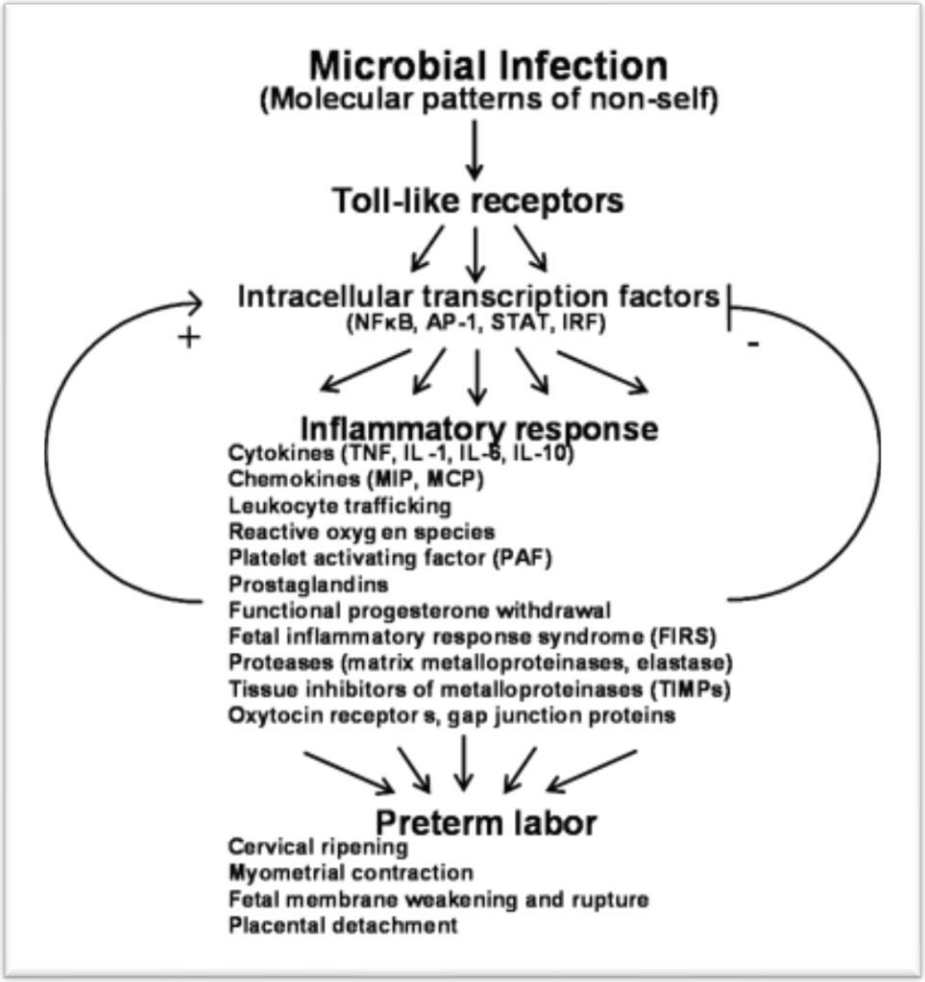

Figure 1. Simplified patophysiology of infection causing preterm labor[6]

Infectious diseases are often diagnosed following cultures of samples isolated from the infection site. A culture is a way of growing a microbe in a laboratory setting. The precise characteristics of the growing culture can be used to identify the specific microbe. Use of a "selective agent" can be used to determine features of the microbe. For example, growth of *Staph aureus*in a culture that contains methicillin (the selective agent) would be indicative of methicillin-resistant *Staph aureus* or MRSA[7].

There are three main types of cultures[8]:

1. **Solid culture.** Bacteria and fungi can grow on a solid surface made of a mix of nutrients, salts and agar (a gelling agent isolated from seaweed). A single microbe placed on the solid surface can grow into colonies or individual groups comprised of thousands of cells. Colonies are made up of clones, in which all cells are identical to each other. This feature is what makes solid cultures so useful for microbial identification. Different kinds of colonies from various species will have distinct traits and characteristics (e.g., color, size, shape and growth rate of the colony), which help microbiologists identify the microbe.
2. **Liquid culture.** A liquid culture is grown in "media" or a "broth" of nutrients. Microbial growth is observed for how quickly the broth becomes cloudy. A cloudier broth typically means a greater number of microbes. Liquid cultures can often contain multiple microbial species, so they tend to be less useful than solid cultures for

diagnosis of bacteria and fungi. Liquid cultures, though, are more useful for diagnosis of parasites, which do not form normal colonies in solid cultures.

3. **Cell culture.** Some microbes, such as Chlamydia or Rickettsia, and viruses cannot be grown in solid or liquid cultures, but can be grown in human or animal cells. Cultures of human or animal cells are used by "infecting" the cell culture with the microbe and observing the effect on the cells. For example, many viruses have detrimental or "cytopathic" effects on the cells that can be observed by microbiologists. Since cell culture methods tend to be more specialized and require more work and longer periods for diagnosis, though, cell culture is usually used secondarily to other diagnostic methods.

Depending on the particular type of culture, the ingredients will vary. In general, most cultures will require a combination of the following[7].

- Amino-nitrogen source (digested proteins)
- Growth factors (blood, serum or yeast extract)
- Energy source (sugars, carbohydrates)
- Salts for buffering pH (phosphate, citrate)
- Minerals (calcium, magnesium or iron)
- Selective agents (antibiotics or chemicals)
- Indicators or dyes (for determining acidity levels)
- Gelling agent for solid cultures (agar)

Urinalysis is the physical, chemical, and microscopic examination of urine. It involves a number of tests to detect and measure various compounds that pass through the urine. The urine sample is examined under a microscope to look at cells, urine crystals, mucus, and other substances in the sample, and to identify any bacteria or other germs that might be present[9].

Microscopic examination of an uncentrifuged Gram-stained urine drop constitutes one of the best diagnostic methods for detecting significant bacteriuria, i.e., the presence of 100,000 or more microorganisms per ml of urine. Observation of one or more bacteria per oil immersion field correlates with 90% of cases of significant bacteriuria.

Microscopic examination without gram staining need can be carried out to diagnose urinary tract infection but have to be accompanied by leukocyte count[10].

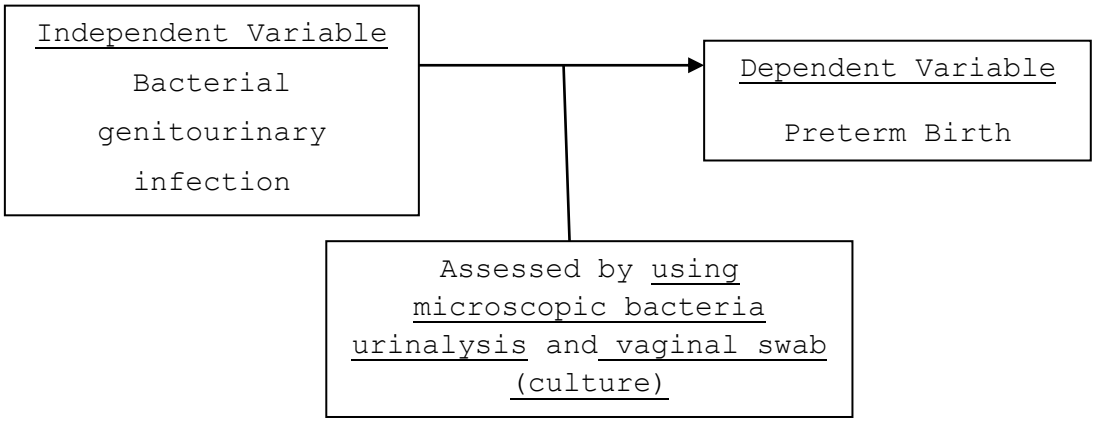

Figure 2. Conceptual Framework

2. Research Method

This research is a prospective observational study with high similarity with diagnostic test in the exception that this study uses the occurrence of preterm birth itself as the so-called gold standard.

Pregnant women within the Yogyakarta province with gestational age of 23 weeks or above (until before labor) and maximum estimated day of birth in the month of February 2012 is obtainable for the study. Pregnant mothers with preterm birth due to Cesarean Section are excluded.

This research is short in preterm samples if compared to non preterm samples. Another limitation is regarding the lab procedure which is prone to contamination due to the setting of the study (community based).

3. Results

During the study period of time, 104 subjects with the characteristics explained in the table are obtained. Where 68 of the subjects had either aterm or post term birth and 36 subjects experience a preterm birth.

Table 2: Participants characteristics, obstetrical profiles, habits and demographics

Characteristics	**Preterm Birth (n=42) n (%)**	**Control (n=76) n (%)**	**OR**	**95% CI**	***P***
Age					
Range					
<20	11 (64.7)	6 (35.3)	5.8	1.56-21.33	0.022
20-24	12 (46.2)	14 (53.8)	2.7	0.85-8.49	
25-29*	7 (24.1)	22 (75.9)	(1.0)		
30-34	7 (30.4)	16 (69.6)	1.4	0.40-4.70	
≥35	5 (21.7)	18 (78.3)	0.9	0.24-3.22	
Marital status					
Married	42	75			
Single	0	1			
Pre-pregnancy BMI[1] (kg/m^2)					
Range					
≤ 18	11 (37.9)	18 (62.1)	1.1	0.44-2.64	0.941
18-25*	25 (36.2)	44 (63.8)	(1.0)		
> 30	4 (28.6)	10 (71.4)	0.7	0.20-2.48	
Missing	2	4			
Obstetrical profile					
Parity					
0	27 (41.50	38 (58.5)	1.8	0.80-4.21	0.443
1-2*	12 (27.9)	31 (72.1)	(1.0)		
≥3	3 (33.3)	6 (66.7)	1.3	0.28-6.01	
Missing		1			
Current twin pregnancy					
Yes	3 (60.0)	2 (40.0)	2.8	0.46-17.76	0.244
No*	39 (34.5)	74 (65.5)	(1.0)		
Hypertension (SBP > 140mmHg)					
Yes	3 (37.5)	5 (62.5)	0.9	0.25-4.82	0.907
No*	39 (35.5)	71 (64.5)	(1.0)		
Previous preterm delivery					
Yes	5 (83.3)	1 (16.7)	10.1	1.14-89.9	0.012
No*	37 (33.0)	75 (67.0)	(1.0)		

Previous abortion					
Yes	3 (18.8)	13 (81.3)	0.4	0.10-1.39	0.130
No*	39 (38.2)	63 (61.8)	(1.0)		
Habits					
Smoking					
Yes	1 (33.3)	2 (66.7)	0.9	0.08-10.26	0.934
No*	41 (35.7)	74 (64.3)	(1.0)		
Drinking alcohol					
Yes	0 (0)	1 (100.0)			
No	42 (35.9)	75 (64.1)			
Illicit drug use					
Yes	0 (0)	0 (0)			
No	0 (0)	0 (0)			
Demographics					
Years of formal education of mother					
Primary					
Junior high school	6 (25.0)	18 (75.0)	0.4	0.14-1.18	0.064
Senior high school	5 (19.2)	21 (80.8)	0.3	0.10-0.88	
Higher education	26 (44.8)	32 (55.2)	(1.0)		
	5 (50.0)	5 (50.0)	1.2	0.32-4.71	
Occupation of mother					
Unemployed*					
Labour, farmer	30 (36.6)	52 (63.4)	(1.0)	0.11-3.05	0.808
Others[2]	2 (25.0)	6 (75.0)	0.6	0.39-2.35	
	10 (35.7)	18 (64.3)	0.9		
Social support during pregnancy					
Yes*				0.46-17.8	
No	39 (34.5)	74 (65.5)	(1.0)		0.244
	3 (60.0)	2 (40.0)	2.8		

1 BMI is an abbreviation for Body Mass Index
2 Others refer to employee, self business, police and teacher

Table 3: 2x2 table showing specifity, sensitivity, PPV and NPV for bacteriuria in detecting preterm birth

		Birth Outcome		Total
		Preterm	Non preterm	
Bacteriuria	+ve	13	45	58
	-ve	23	23	46
Total		36	68	104

From the table above, it is obtained that the bacteria urinalysis has sensitivity 36.1%, specificity 33.8%, positive predictive value (PPV) 22.4% and negative predictive value (NPV) 50%.

Table 4: 2x2 table showing specifity, sensitivity, PPV and NPV for vaginal swab culture in detecting preterm birth

		Birth1		Total
		Preterm	Non Preterm	
Bacteria in vaginal swab culture	+ve	17	13	30
	-ve	19	55	74
Total		36	68	104

From the table above it is obtained that vaginal swab culture in predicting for preterm birth has sensitivity of 47.2%, specificity of 80.8%, positive predictive value 56.6% and negative predictive value of 74.3%.

These findings can be summarized in the table below:

Table 5: summary of the two prediction tool accuracy

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Bacteria urinalysis	36.1	33.8	22.4	50
Vaginal swab culture	47.2	80.8	56.6	74.3

4. Discussion

Genital infection has been long proven to be a major risk factor for preterm birth. The most case of genital infection is Bacterial Vaginosis. In the previous studies mentioned in the first chapter, where they use the diagnosis of Bacterial Vaginosis to detect preterm birth, also shows similar results as the vaginal swab culture which is more likely due to genital infection rather than the urinary tract infection. Both shows low sensitivity, but high specificity and also low positive predictive value but high negative predictive value. This is useful for high risk pregnant women to assure their possibility in experiencing a preterm labor. Due to its low sensitivity, vaginal swab culture is not recommended to be use routinely moreover in low-risk pregnant women.

As for urinalysis, due to its low specificity and sensitivity is not recommended to be used to predict preterm birth. Urinalysis is actually very prone to contamination, moreover in the community setting. Thus, without being used for predicting birth, bacteria urinalysis has been said to have low sensitivity to diagnose urinary tract infection.

5. Conclusion

Urinalysis has not been proven to be useful in predicting preterm birth. In the other hand, vaginal swab culture can be useful in ruling out preterm birth occurrences especially in high-risk pregnant women.

6. Recommendations

Since vaginal swab culture can be obtained in district hospital, women with high-risk of experiencing preterm labor might benefit from this test. Thus, if the couple is categorized low-income, high-risk mothers should start to be more aware on their activities as well as their nutrition.

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