

THE MEASUREMENT OF URINARY PYRIDINIUM CROSSLINKS AS A SENSITIVE BIOMARKER OF NUTRITIONAL STATUS IN ADOLESCENTS

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Abstract

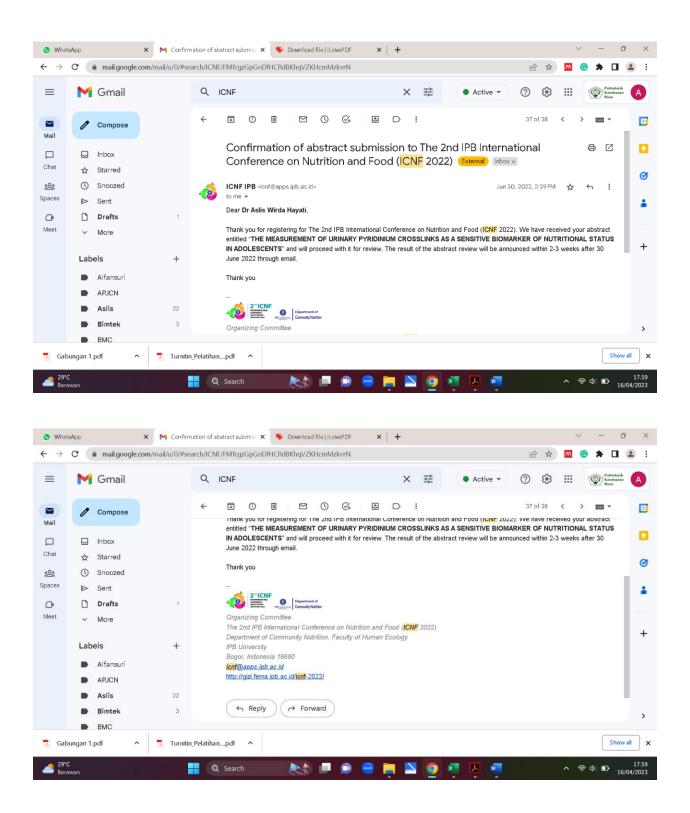
The study's purpose was to compare anthropometric method of measuring nutritional status with the height for age z-score (HAZ) by measuring biochemical content of urinary Pyridinium crosslinks (Pyd). The research design was a quasi-experimental pre and posttest, conducted at SMPN 1 Kampar (Junior High School), Riau Province. The research samples were students aged 12-15 years as many as 76 respondents consisting of normal and stunted adolescents. Provision of nutritional intervention in the form of a midmorning snack with an energy content of 575.1 kcal was conducted in January-March 2022. Pyd content was analyzed using MicroVue™ PYD EIA kit, USA, while the data were analyzed using Anova test. The HAZ's students with normal status before and after intervention had the same value (0.65±0.70 and -0.67±0.69; p>0.05), as well as students with stunted status, namely HAZ values before and after nutrition intervention had the same value (-2.32±0.36 and -2.29±0.35; p>0.05); However, the HAZ's adolescent with normal and stunted status was different (p<0.05). Therefore, it indicated that the provision of nutritional intervention did not improve the nutritional status of adolescents from stunted to normal. Besides, it was found that Pyd content was normal both before and after of nutrition intervention (140.41±70.35 and 122.28 ±72.72 nmol/mmol creatinine), which meant different from the stunted adolescents before the nutrition intervention (191.65±69.58 nmol/mmol creatinine); but Pyd content of stunted adolescents after nutritional intervention (158.47±58.84 nmol/mmol creatinine) was same with Pyd content of normal adolescents (p<0.05). It signified that the provision of nutritional interventions can improve the nutritional status of stunted adolescents to normal. It can be concluded that the measurement of stunting nutritional status using Pyd is more sensitive than anthropometric of HAZ. The further research is needed on the cutoff point value of stunting nutritional status in adolescents with larger samples in an epidemiological research scale.

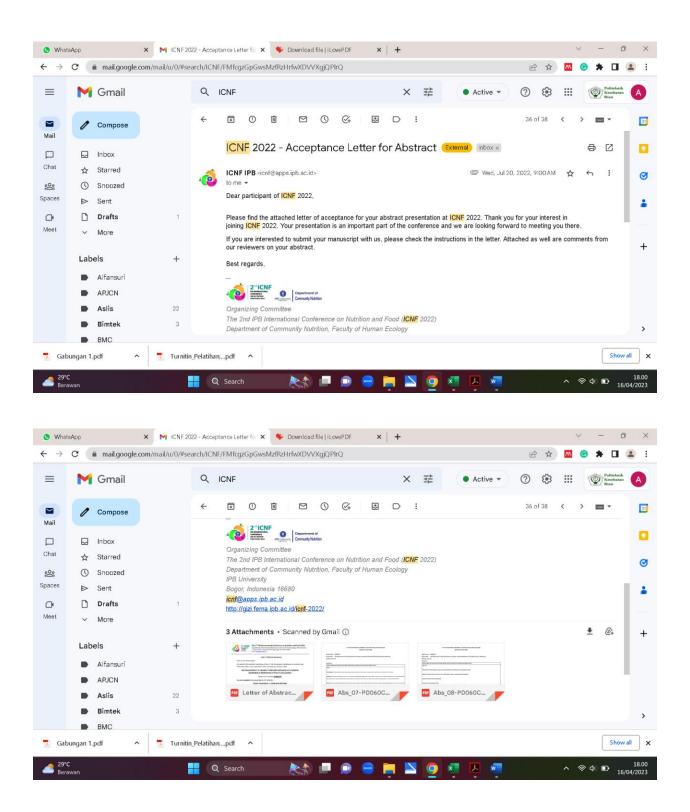
Keywords: Urine Pyridinium crosslinks, Sensitivity, Anthropometry, Biomarker, Nutritional status

Tujuan penelitian yaitu untuk membandingkan cara pengukuran status gizi secara antropometri nilai z-score TB/U dengan secara biokimia kandungan Pyridinium crosslinks (Pyd) urin. Disain penelitian vaitu quasi eksperimen pre dan post test. Penelitian dilakukan di SMP Negeri 1 Kampar Propinsi Riau. Sampel penelitian yaitu remaja usia 12 – 15 tahun sebanyak 76 orang yang terdiri dari remaja normal dan stunting. Pemberian intervensi gizi berupa midmorning snack dengan kandungan energi 575.1 kkal pada Januari-Maret 2022. Kandungan Pyd urin dianalisis menggunakan MicroVueTM PYD EIA kit, USA. Data dianalsis menggunakan Anova. Nilai z-score TB/U responden dengan status gizi normal sebelum dan setelah intervensi gizi adalah sama (-0.65 ± 0.70 dan -0.67 ± 0.69 ; p>0.05), begitu juga dengan responden dengan status gizi stunting yaitu nilai z-score TB/U sebelum dan setelah intervensi gizi adalah sama (- 2.32 ± 0.36 dan -2.29 ± 0.35 ; p>0.05); namun nilai z-score TB/U responden dengan status gizi normal dan responden dengan status gizi stunting adalah berbeda (p<0.05). Artinya, pemberian intervensi gizi tidak meningkatkan status gizi responden dari stunting menjadi normal pada penilaian secara antropometri z-score TB/U. Di sisi lain dengan pengukuran secara biokimia diketahui bahwa kandungan Pyd urin responden normal baik sebelum intervensi maupun sesudah intervensi gizi (140.41±70.35 dan 122.28 ±72.72 nmol/mmol creatinine) adalah berbeda dengan responden stunting sebelum intervensi gizi (191.65±69.58 nmol/mmol creatinine); namun kandungan Pyd urin responden stunting setelah intervensi gizi (158.47±58.84 nmol/mmol creatinine) menjadi sama dengan kandungan Pyd urin responden dengan status gizi normal (p<0.05). Artinya, pemberian intervensi gizi dapat meningkatkan status gizi responden stunting menjadi normal pada penilaian status gizi menggunakan biomarker Pyd urin. Terlihat bahwa penilaian status gizi stunting dengan menggunakan kandungan Pvd urin lebih sensitif dibandingkan secara antropometri z-score TB/U. Perlu dilakukan penelitian lanjutan tentang nilai cut off point status gizi stunting melalui kandungan Pyd urin pada remaja dengan jumlah sampel yang lebih besar dalam skala penelitian epidemiologi.

Keyword: Pyridinium crosslinks urin, sensitifitas, antropometri, biomarker, status gizi

Pyd mempunyai peranan menghubungkan molekul kolagen dengan fibril kolagen dan merupakan penguat mekanik tulang. Pyd dilepas ke dalam sirkulasi dan di ekskresi ke urin dalam bentuk bebas (±40%) dan terikat dengan peptida (±60%). Ekskresi Pyd di urin merupakan parameter yang baik untuk resepsi tulang. Metode mengukur Pyd crosslink antara lain adalah HPLC (High pressure liquid chromotography) dan ELISA. Pemeriksaan Pyd crosslink di urin spesifik untuk tulang dan digunakan sebagai petanda resorpsi tulang serta memperkirakan risiko terjadinya patah tulang (Widijanti, dkk. 2003)





2nd IPB INTERNATIONAL CONFERENCE ON NUTRITION AND FOOD (ICNF 2022) ABSTRACT REVIEW FORM

Abstract code : PD060COX

Abstract title : The Measurement of Urinary Pyridinium Crosslinks as a Sensitive Biomarker of Nutritional Status in Adolescents

Reviewer name: 07

Comments:

Please explain any weak areas and offer specific advice as to how the author(s) may improve them.

Title: -

Introduction: Please provide a short introduction that describes the main subject, purpose, the importance, and context of the research.

Methods: The research design was not in line with the title and purpose/objective of the research. If you want to compare anthropometric measurement with Pyd, why did you use quasi experimental study, not cross-sectional? Why did you use Anova, there was only two groups (i.e., normal and stunted)?

Results: Not comprehensible. The first few sentences discuss that the intervention did not improve the nutritional status of adolescents. This is not in line with the objective of the study. The second part regarding the Pyd result could not be understood:

- Besides, it was found that Pyd content was normal both before and after of nutrition intervention (140.41±70.35 and 122.28 ±72.72 nmol/mmol creatinine) → are these the total average of both normal and stunted group?
- which meant different from the stunted adolescents before the nutrition intervention (191.65±69.58 nmol/mmol creatinine) → different from normal nutritional status?
- but Pyd content of stunted adolescents after nutritional intervention (158.47±58.84 nmol/mmol creatinine) was same with Pyd content of normal adolescents (p<0.05) → how much is Pyd content of normal nutritional status? How could you say it's the same if p<0.05?
- It signified that the provision of nutritional interventions can improve the nutritional status of stunted adolescents to normal → based on which result?

Conclusions: It is a jumping conclusion. It's not clear which result is the base for this conclusion. How could you say Pyd was more sensitive than HAZ to measure stunting, while HAZ is the gold standard for measuring stunting?

Keywords: Please provide keywords different from the words used in the title

Language: Some contents are not comprehensible. Too wordy and long sentences in result. Please proofread.

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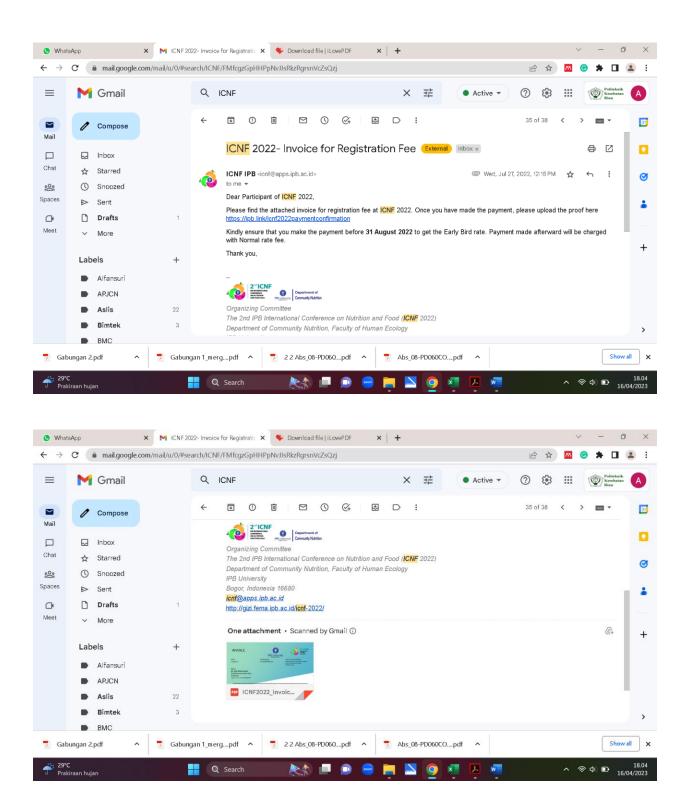
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Title: OK
Introduction: No links between why use Urinary Pyridinium Crosslinks for the assessment of HAZ
Methods: Should include more info on the intervention study i.e. randomication, blinding etc
Results: Not clear and very confusing
Conclusions, Not an esific to UA7
Conclusions: Not specific to HAZ
Keywords: -
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Language: Contradicting statements

ABSTRACT

The study's purpose was to compare anthropometric method of measuring nutritional status with the height for age zscore (HAZ) by measuring biochemical content of urinary Pyridinium crosslinks (Pyd). The research design was a quasiexperimental pre and posttest, conducted at SMPN 1 Kampar (Junior High School), Riau Province. The research samples were students aged 12-15 years as many as 76 respondents consisting of normal and stunted adolescents. Provision of nutritional intervention in the form of a midmorning snack with an energy content of 575.1 kcal was conducted in January-March 2022. Pyd content was analyzed using MicroVue™ PYD EIA kit, USA, while the data were analyzed using Anova test. The HAZ's students with normal status before and after intervention had the same value (0.65±0.70 and -0.67±0.69; p>0.05), as well as students with stunted status, namely HAZ values before and after nutrition intervention had the same value (-2.32±0.36 and -2.29±0.35; p>0.05); However, the HAZ's adolescent with normal and stunted status was different (p<0.05). Therefore, it indicated that the provision of nutritional intervention did not improve the nutritional status of adolescents from stunted to normal. Besides, it was found that Pyd content was normal both before and after of nutrition intervention (140.41±70.35 and 122.28 ±72.72 nmol/mmol creatinine), which meant different from the stunted adolescents before the nutrition intervention (191.65±69.58 nmol/mmol creatinine); but Pyd content of stunted adolescents after nutritional intervention (158.47±58.84 nmol/mmol creatinine) was same with Pyd content of normal adolescents (p<0.05). It signified that the provision of nutritional interventions can improve the nutritional status of stunted adolescents to normal. It can be concluded that the measurement of stunting nutritional status using Pyd is more sensitive than anthropometric of HAZ. The further research is needed on the cutoff point value of stunting nutritional status in adolescents with larger samples in an epidemiological research scale.

Keywords: Urine Pyridinium crosslinks, Sensitivity, Anthropometry, Biomarker, Nutritional status



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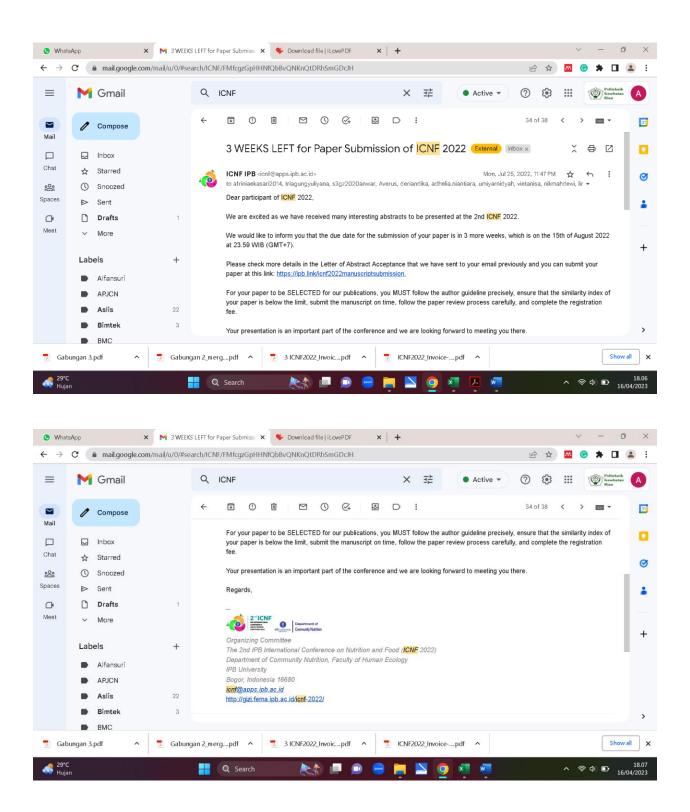
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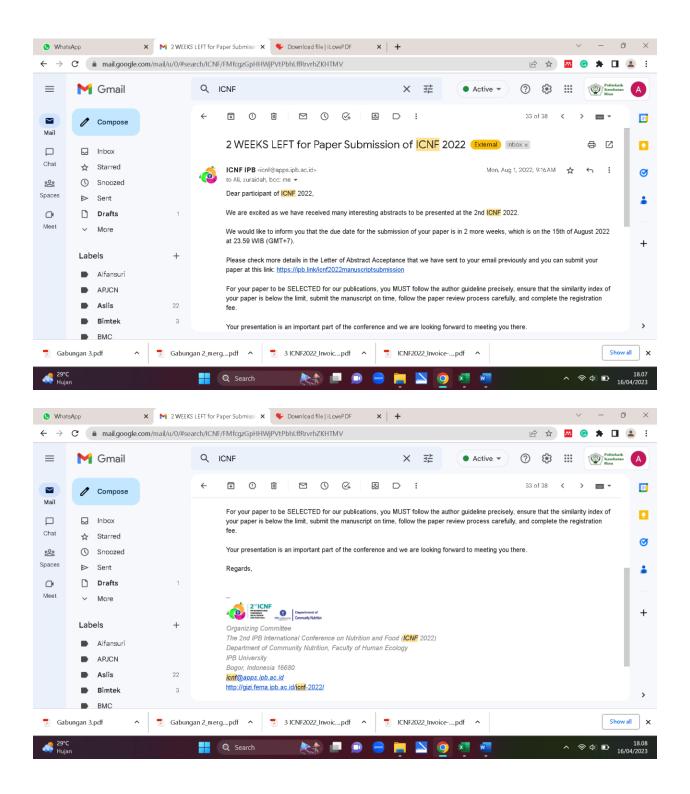
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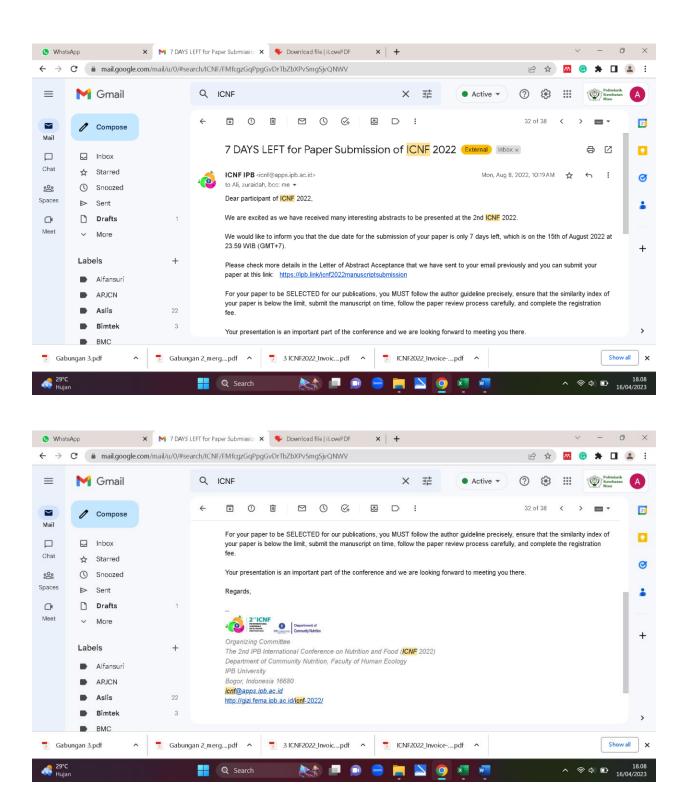
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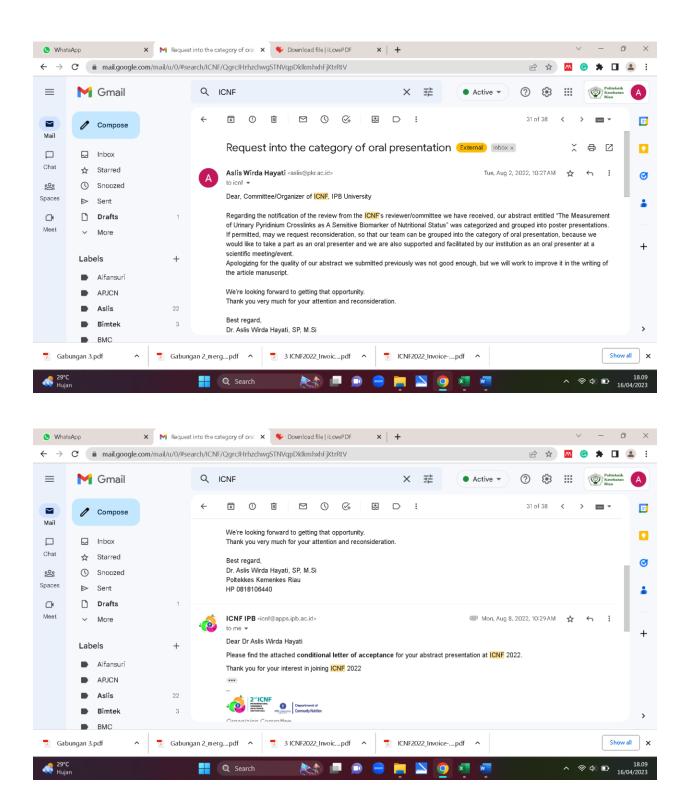
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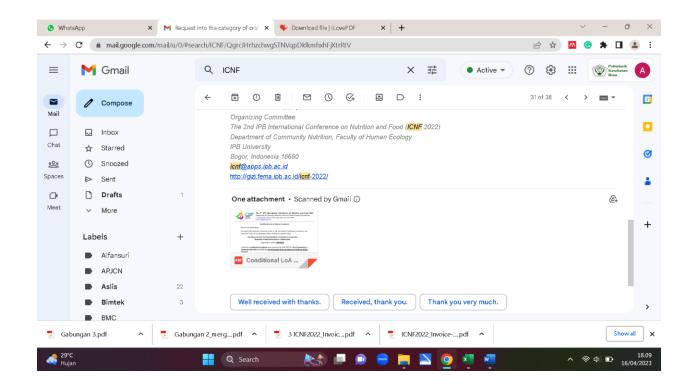
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Conditional Letter of Abstract Acceptance

Dear Dr Aslis Wirda Hayati

On behalf of the Scientific Committee of the 2st IPB International Conference on Nutrition and Food (ICNF 2022), we are pleased to inform you that your abstract titled:

The Measurement of Urinary Pyridinium Crosslinks as A Sensitive Biomarker of Nutritional Status in Adolescents

(Registration number PD060COO)

is offered a **conditional acceptance** to be presented at ICNF 2022 for **Oral Presentation** in **Community Nutrition** provided that the manuscript that you submit can fulfill our quality standard.

If you wish to publish your research paper with us as a proceeding in the format of **Extended Abstract** that will be published in a supplementary issue with the <u>Malaysian Journal of Medicine</u>

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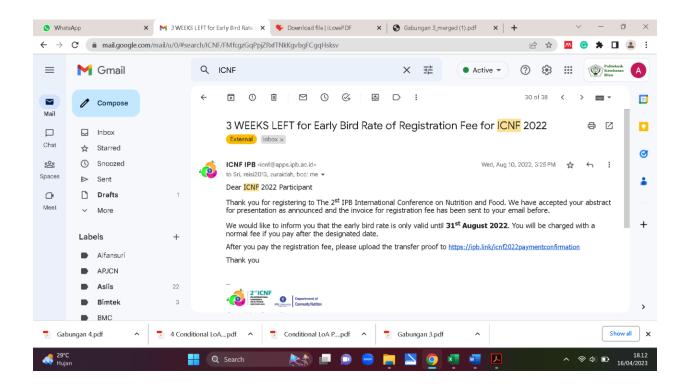
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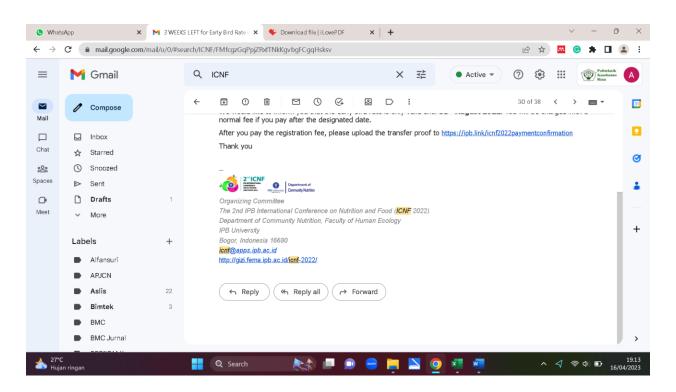
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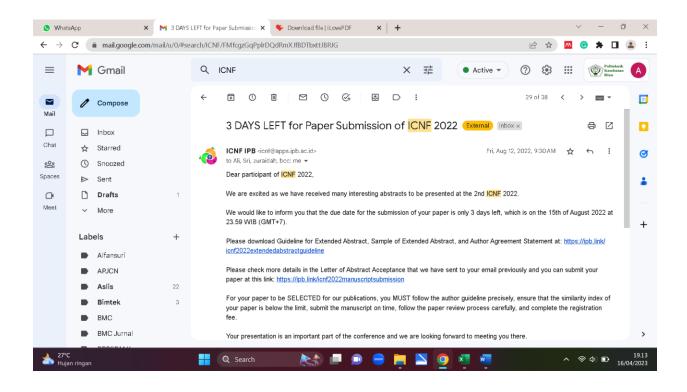
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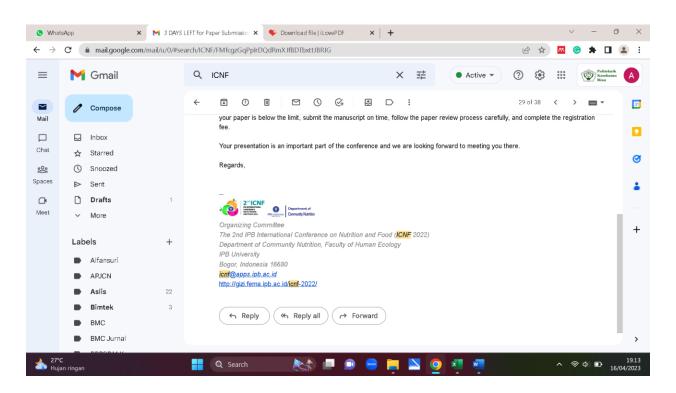
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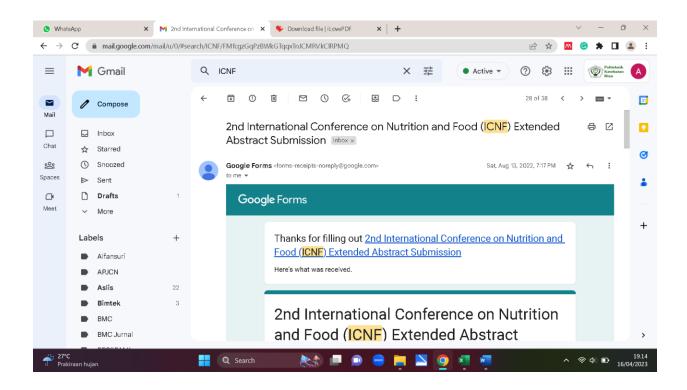
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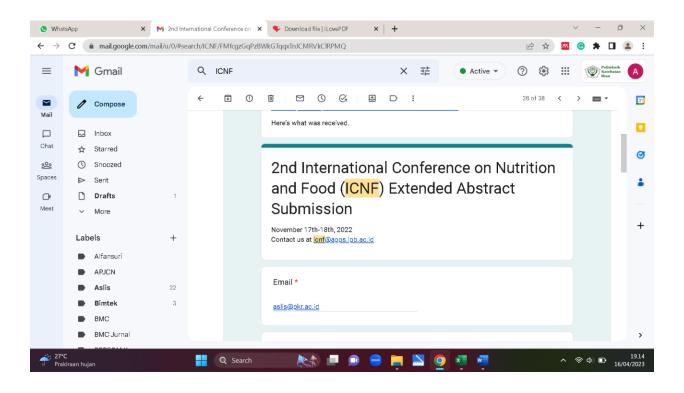


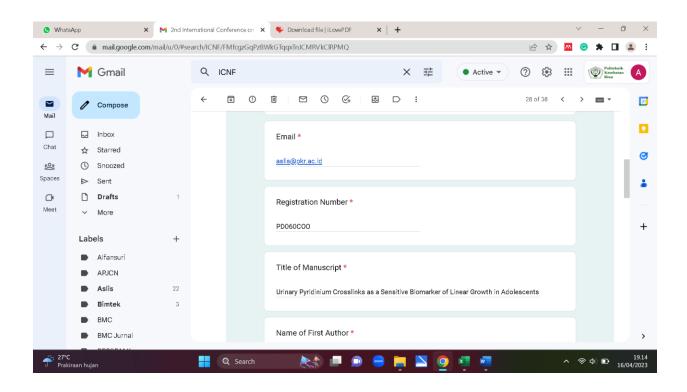


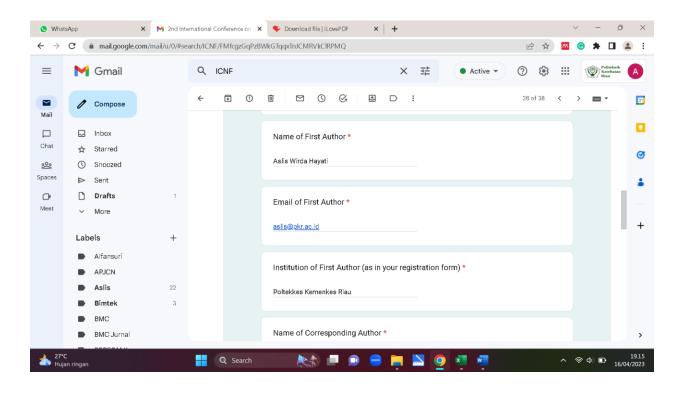


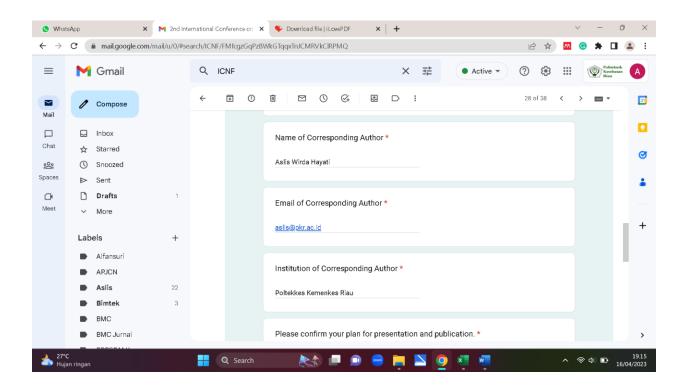


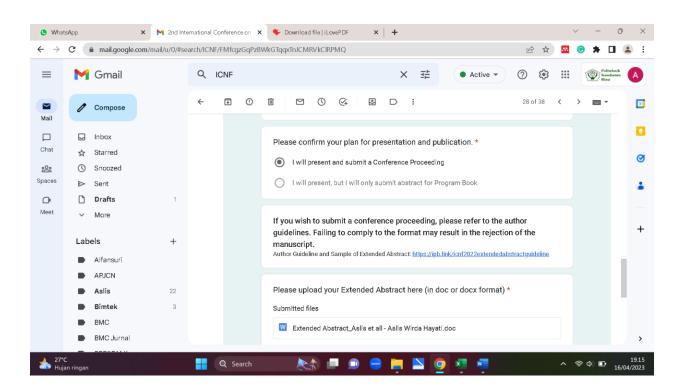


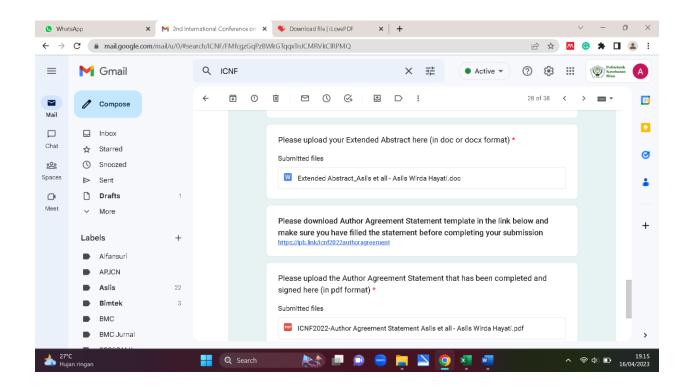


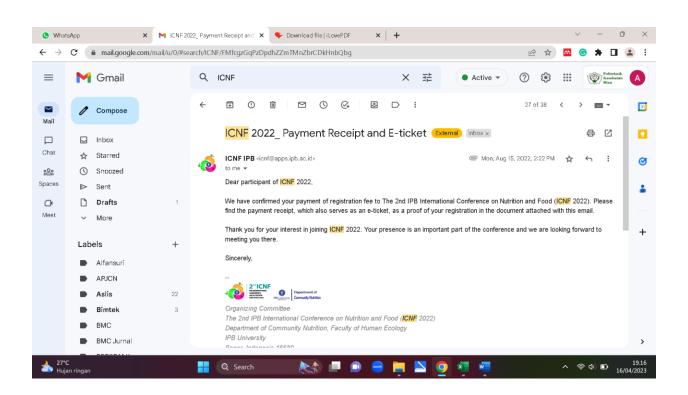


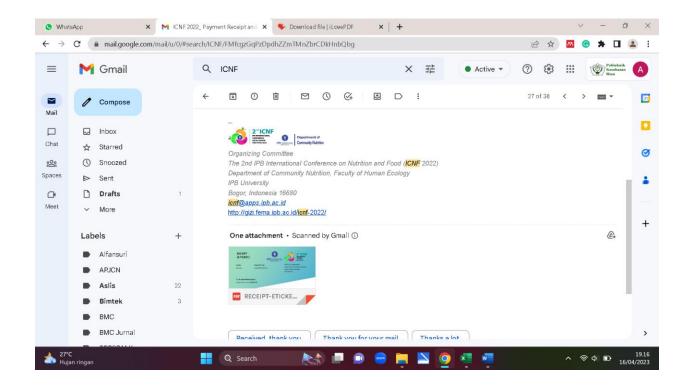


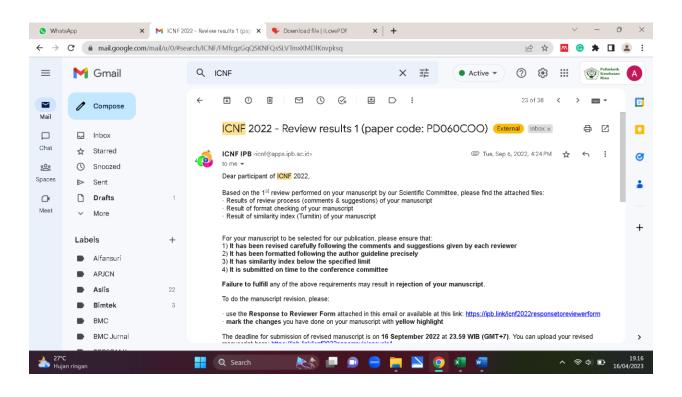


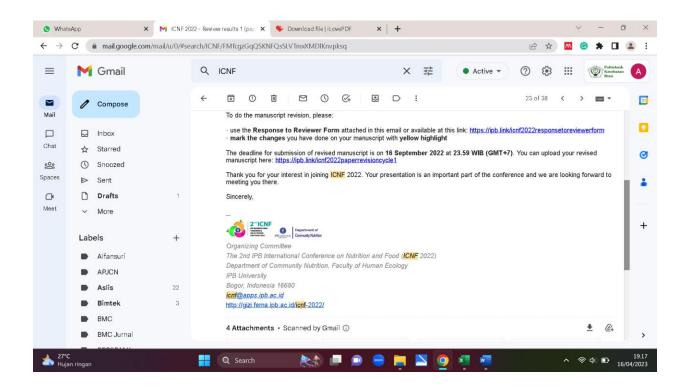


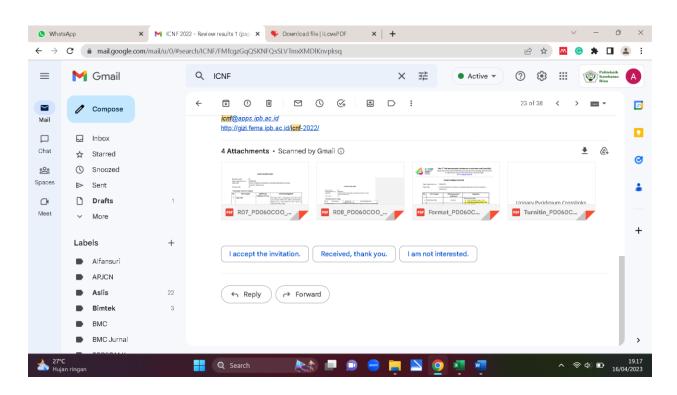












PAPER REVIEW FORM

Reviewer code : 07

Paper registration no. : PD060COO

Paper title : Urinary Pyridinium Crosslinks as a Sensitive Biomarker of Linear

Growth in Adolescents

Review cycle : 01

*total pages maximum 3 pages

No.	Part of paper	Specific sub-	Comment/Suggestion		
		heading or line no.			
1	Paper title		The paper title is misguiding, since the result only showed difference before intervention. Please give a title based on the result or objective of the study.		
2	 Summary Max 100 words Contains introduction, method, results, and conclusion 		No conclusion. Method is not clear, what kind of nutrition intervention. How long was the intervention.		
3	Keywords - Max. 5 words/phrases - Relevant to content		The first keyword is too long.		
4	Introduction - Max 150 words - Contains background, research gap, and objectives		Please state the objective of this study. The explanation on Pyd urine could be deliver more concise.		
5	Materials and Methods - Max 150 words	Line 36-38	There should be 2 intervention groups \rightarrow those who received the snack and milk and the control group. What intervention was given to the control group? Then before and after the intervention the 4 indicators of linear growth were evaluated and compared.		
		Line 40	What is the snack given to the subjects? How long was the intervention (in days/weeks/months)?		
		Line 41	Microtoa → microtoise		
		Line 43	At what time were urine collected? First urine in the morning or else?		
		Line 47	The analysis were paired samples. Could Anova be used for this type of analysis?		
6a	Results and Discussion - Max 300 words	Line 52	Radiological bone mass \rightarrow in the method it is stated that bone mass was obtain from a Sylim model scale, not radiological examination.		
6b	Tables/ Graphs - Max 3	_	Should be analyse again since the design of study is not suited for this study (please see comment on the intervention groups in the		

		method section)
7	Conclusions	The conclusion is misguiding, not in
	- Max 50 words	accordance with the objective.
8	Acknowledgements	-
	(optional)	
9	List of references	Please use references not older than 10 years.
	- Max 5	
10	Other aspects	
	- Language	
	 (filled by reviewer as needed) 	

Date of review completion: September 1, 2022

Urinary Pyridinium Crosslinks as a Sensitive Biomarker of Linear Growth in Adolescents

Summary

Urinary pyridinium crosslinks (Pyd) is a sensitive biomarker of linear growth. This study evaluated the sensitivity of four linear growth indicators: height, body energy, bone mass, and Pyd urine. This study measured linear growth in stunted and normal adolescents before and after nutrition intervention. There was no difference in average results of nutrition interventions on linear growth among groups of adolescents using bone mass and body energy indicators. The change in adolescents' height was not convincing through measuring efficacy of nutrition interventions. The Pyd urine of stunted adolescents before nutrition intervention was significantly different from Pyd urine of normal adolescents.

Keywords

Efficacy of nutritional intervention measurement, Height, Pyridinium crosslinks, Biomarker of stunting, Midmorning snack

Introduction

The rapidly usable and convincing indicators are needed to measure efficacy of nutrition interventions related to linear growth (1). The current linear growth indicator is height (2). This indicator takes a long time to produce results from nutrition interventions and the results are not convincing. The duration of providing nutrition interventions to malnourished children (4-15 yo) to increase linear growth is 18 months to find out significant results (3). Other indicators are body energy, bone density, and Pyd urine. The two main cell types, responsible for bone renewal, are osteoblasts involved in bone formation and osteoclasts involved in bone resorption. The balance among those dictates net bone remodeling (4). Osteoclasts will absorb bone in about 3 weeks to form tunnels with length of several millimeters. After 3 weeks, osteoblasts begin to form new bone which lasts for several months. Osteoclastic cells dissolve Pyd and release it into the urine (5).

Materials and Methods

The research design was a quasi-experimental pre-post test. The samples were 78 selected teenagers (12-15 yo) at SMPN 1 Kampar in Riau Province. There were four treatment groups: stunted respondents before and after nutrition intervention, normal respondents before and after nutrition intervention. The indicators of nutrition status were height, bone mass, body energy, and Pyd urine. As nutritional interventions, midmorning snack and milk were given in January to March 2022 (as additional energy; 30% recommended dietary allowance). Height gauges (microtoa) used STATURE METER 2M GEA. Bone mass and body energy were measured by using Sylim Model Scale No. BFS 712PH. Urines were collected with sterile urine container of OneMed 60ml. Adolescents' urines were collected by Prodia. Analysis of urine samples was carried out by Prodia Center in Jakarta. Measurements of Pyd were performed with the use of MicroVue™ PYD EIA kit, using a Spectrophotometer. Anova was applied for statistical analysis.

Result and Discussion

Measuring efficacy of nutrition interventions on linear growth of adolescents by using Pyd urine biomarker was more sensitive than anthropometric height, food intake energy of body, and radiological bone mass. There was no difference in average results of linear growth among groups of adolescents on body energy and bone mass (p> 0.01); Conversely, there was a difference in average results of linear growth among groups of adolescents on height and Pvd urine (p<0.01) (Table 1). The average changes in height of stunted and normal adolescents before and after nutrition intervention, respectively, were 0.95±0.64 and 0.82±0.83 cm. The change in height, less than 1 cm, was not convincing in measuring efficacy of nutrition interventions. The average changes in Pyd urine of stunted and normal adolescents before and after nutrition intervention, respectively, were 44.80±91.36 and 12.34±76.10 nmol/mmol creatinine. The change in Pyd urine was more convincing than height in measuring efficacy of nutrition interventions. The average Pyd urine of stunted adolescents before nutrition intervention was different from normal after nutrition intervention (p<0.01). The Pyd urine of stunted adolescents before intervention was 182.84±71.70 nmol/mmol creatinine, while the Pvd of normal adolescents after nutrition intervention was 124.31±73.48 nmol/mmol creatinine. The average results on linear growth using Pvd urine indicator showed the provision of nutrition interventions can improve nutritional status of stunted adolescents to normal, and did not convert nutritional status of normal adolescents. The number of stunted adolescents before nutrition intervention was 29 adolescents and decreased after the nutrition intervention to 27. The use of Pyd urine biomarkers revealed the provision of nutrition interventions could improve nutritional status of Pyd from stunted to normal by 7.4% (n=27). Therefore, the Pyd urine is expected to be a marker of the efficacy of nutritional care in bone growth disorders associated with bone resorption in stunted adolescents.

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Table 1. Indicators of Linear Growth in Measuring Efficacy Results of Nutrition Intervention

Variable	Treatment	n	Mean	р
HAZ				0,000
	Stunting before nutrition intervention	29	-2,3±0,4 ^a	
	Stunting after nutrition intervention	28	-2,3±0,3 ^a	
	Normal before nutrition intervention	48	-0,6±0,7 ^b	
	Normal after nutrition intervention	49	-0.7 ± 0.7^{b}	
	Total	154	-1,3±1.0	
Height (cm)				0,000
- '	Stunting before nutrition intervention	29	146,5±4,8 ^a	
	Stunting after nutrition intervention	28	147,4±4,8 ^a	
	Normal before nutrition intervention	48	157,9±6,1 ^b	
	Normal after nutrition intervention	49	158,6±6,0 ^b	
	Total	153	154,1±7,8	
Bone mass (%)				0,807
	Stunting before nutrition intervention	22	12,0±2,0 ^a	
	Stunting after nutrition intervention	20	11,7±2,1 ^a	
	Normal before nutrition intervention	43	12,0±2,1 ^a	
	Normal after nutrition intervention	45	12,2±2,1 ^a	
	Total	130	12,0±2,1 ^a	
Energy of body (Kcal)				0,294
	Stunting before nutrition intervention	22	1826±220 ^a	
	Stunting after nutrition intervention	20	1828±239 ^a	
	Normal before nutrition intervention	45	2056±296a	
	Normal after nutrition intervention	45	2073±310 ^a	
	Total	132	1989±300	
Pyd (nmol/mmol creatinine)				0,006
•	Stunting before nutrition intervention	29	182,8±71,7 ^a	
	Stunting after nutrition intervention	27	152,1±61,1 ^{ab}	
	Normal before nutrition intervention	47	142,6±71,6 ^{ab}	
	Normal after nutrition intervention	49	124,3±73,5 ^b	
	Total	152	146,1±72,8	

NOTE: Mean \pm SD; p < 0.01 for significance of ANOVA; ab p < 0.05 for significance of Duncan

Conclusions

 The Pyd urine of stunted adolescents decreased after being given nutrition intervention and could indicate an improved nutritional status; while the normal adolescents' Pyd urine also decreased and remained in normal nutritional status. This study revealed that Pyd can be used as a sensitive biomarker of linear growth in adolescents.

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PAPER REVIEW FORM

: 08 Reviewer code

Paper registration no. : PD060COO
Paper title : Urinary Pyri : Urinary Pyridinium Crosslinks as a Sensitive Biomarker of Linear Growth in Adolescents

Review cycle :01

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No.	Part of paper	Specific sub-	Comment/Suggestion
	• •	heading or line no.	. 33
1	Paper title	<u> </u>	The paper title is misguiding, since the result only showed difference before intervention. Please give a title based on the result or objective of the study.
2	 Summary Max 100 words Contains introduction, method, results, and conclusion 		No conclusion. Method is not clear, what kind of nutrition intervention. How long was the intervention.
3	Keywords - Max. 5 words/phrases - Relevant to content		The first keyword is too long.
4	Introduction - Max 150 words - Contains background, research gap, and objectives		Please state the objective of this study. The explanation on Pyd urine could be deliver more concise.
5	Materials and Methods - Max 150 words	Line 36-38	There should be 2 intervention groups \rightarrow those who received the snack and milk and the control group. What intervention was given to the control group? Then before and after the intervention the 4 indicators of linear growth were evaluated and compared.
		Line 40	What is the snack given to the subjects? How long was the intervention (in days/weeks/months)?
		Line 41	Microtoa → microtoise
		Line 43	At what time were urine collected? First urine in the morning or else?
		Line 47	The analysis were paired samples. Could Anova be used for this type of analysis?
6a	Results and Discussion - Max 300 words	Line 52	Radiological bone mass → in the method it is stated that bone mass was obtain from a Sylim model scale, not radiological examination.
6b	Tables/ Graphs - Max 3		Should be analyse again since the design of study is not suited for this study (please see comment on the intervention groups in the

		method section)
7	Conclusions	The conclusion is misguiding, not in
	- Max 50 words	accordance with the objective.
8	Acknowledgements	-
	(optional)	
9	List of references	Please use references not older than 10 years.
	- Max 5	
10	Other aspects	
	 Language (filled by reviewer as needed) 	

Date of review completion: September 1, 2022

Summary

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 Urinary pyridinium crosslinks (Pyd) is a sensitive biomarker of linear growth. This study evaluated the sensitivity of four linear growth indicators: height, body energy, bone mass, and Pyd urine. This study measured linear growth in stunted and normal adolescents before and after nutrition intervention. There was no difference in average results of nutrition interventions on linear growth among groups of adolescents using bone mass and body energy indicators. The change in adolescents' height was not convincing through measuring efficacy of nutrition interventions. The Pyd urine of stunted adolescents before nutrition intervention was significantly different from Pyd urine of normal adolescents.

Keywords

Efficacy of nutritional intervention measurement, Height, Pyridinium crosslinks, Biomarker of stunting, Midmorning snack

Introduction

The rapidly usable and convincing indicators are needed to measure efficacy of nutrition interventions related to linear growth (1). The current linear growth indicator is height (2). This indicator takes a long time to produce results from nutrition interventions and the results are not convincing. The duration of providing nutrition interventions to malnourished children (4-15 yo) to increase linear growth is 18 months to find out significant results (3). Other indicators are body energy, bone density, and Pyd urine. The two main cell types, responsible for bone renewal, are osteoblasts involved in bone formation and osteoclasts involved in bone resorption. The balance among those dictates net bone remodeling (4). Osteoclasts will absorb bone in about 3 weeks to form tunnels with length of several millimeters. After 3 weeks, osteoblasts begin to form new bone which lasts for several months. Osteoclastic cells dissolve Pyd and release it into the urine (5).

Materials and Methods

The research design was a quasi-experimental pre-post test. The samples were 78 selected teenagers (12-15 yo) at SMPN 1 Kampar in Riau Province. There were four treatment groups: stunted respondents before and after nutrition intervention, normal respondents before and after nutrition intervention. The indicators of nutrition status were height, bone mass, body energy, and Pyd urine. As nutritional interventions, midmorning snack and milk were given in January to March 2022 (as additional energy; 30% recommended dietary allowance). Height gauges (microtoa) used STATURE METER 2M GEA. Bone mass and body energy were measured by using Sylim Model Scale No. BFS 712PH. Urines were collected with sterile urine container of OneMed 60ml. Adolescents' urines were collected by Prodia. Analysis of urine samples was carried out by Prodia Center in Jakarta. Measurements of Pyd were performed with the use of MicroVue™ PYD EIA kit, using a Spectrophotometer. Anova was applied for statistical analysis.

Result and Discussion

Commented [A1]: Please improve your title and measuring Pyd as a biomarker for liner growth was not the main interntion of this study.

Commented [A2]: What is this? Please be specific

Commented [A3]: Is this an intervention study? If yes, what was the intervention like?

Commented [A4]: Why not convincing? What are the barriers?

Commented [A5]: Improvement in bone take a long time too!

Commented [A6]: How many months? Be specific!

Commented [A7]: Do you mean 2 groups?

Commented [A8]: Why snack and milk? What were the adherence like?

Commented [A9]: Rephrase

Commented [A10]: rephrase

Commented [A11]: Rephrase

Why anova? Not t-test since only two groups?

Measuring efficacy of nutrition interventions on linear growth of adolescents by using Pyd urine biomarker was more sensitive than anthropometric height, food intake energy of body, and radiological bone mass. There was no difference in average results of linear growth among groups of adolescents on body energy and bone mass (p> 0.01); Conversely, there was a difference in average results of linear growth among groups of adolescents on height and Pyd urine (p<0.01) (Table 1). The average changes in height of stunted and normal adolescents before and after nutrition intervention, respectively, were 0.95±0.64 and 0.82±0.83 cm. The change in height, less than 1 cm, was not convincing in measuring efficacy of nutrition interventions. The average changes in Pyd urine of stunted and normal adolescents before and after nutrition intervention, respectively, were 44.80±91.36 and 12.34±76.10 nmol/mmol creatinine. The change in Pyd urine was more convincing than height in measuring efficacy of nutrition interventions. The average Pyd urine of stunted adolescents before nutrition intervention was different from normal after nutrition intervention (p<0.01). The Pyd urine of stunted adolescents before intervention was 182.84±71.70 nmol/mmol creatinine, while the Pyd of normal adolescents after nutrition intervention was 124.31±73.48 nmol/mmol creatinine. The average results on linear growth using Pyd urine indicator showed the provision of nutrition interventions can improve nutritional status of stunted adolescents to normal, and did not convert nutritional status of normal adolescents. The number of stunted adolescents before nutrition intervention was 29 adolescents and decreased after the nutrition intervention to 27. The use of Pyd urine biomarkers revealed the provision of nutrition interventions could improve nutritional status of Pyd from stunted to normal by 7.4% (n=27). Therefore, the Pyd urine is expected to be a marker of the efficacy of nutritional care in bone growth disorders associated with bone resorption in stunted adolescents.

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76 77 Commented [A12]: How was this determined?

Commented [A13]: Children/adolescents do grow anyway!

Commented [A14]: But this was reflected in overall height improvements? Why so?

Commented [A15]: Is this correct?

Commented [A16]: It can be the marker but not necessarily improves height/stunting!

Table 1. Indicators of Linear Growth in Measuring Efficacy Results of Nutrition Intervention

Variable	Treatment	n	Mean	р
HAZ				0,000
	Stunting before nutrition intervention	29	-2,3±0,4 ^a	
	Stunting after nutrition intervention	28	-2,3±0,3 ^a	
	Normal before nutrition intervention	48	-0,6±0,7 ^b	
	Normal after nutrition intervention	49	-0,7±0,7 ^b	
	Total	154	-1,3±1.0	
Height (cm)				0,000
5 , ,	Stunting before nutrition intervention	29	146,5±4,8 ^a	
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	Normal before nutrition intervention	48	157,9±6,1 ^b	
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	Total	153	154,1±7,8	
Bone mass (%)			- , ,-	0,807
(11)	Stunting before nutrition intervention	22	12,0±2,0 ^a	-,
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	Normal before nutrition intervention	43	12,0±2,1a	
	Normal after nutrition intervention	45	12,2±2,1a	
	Total	130	12,0±2,1 ^a	
Energy of body (Kcal)			,,.	0,294
3, 1 11, (11,	Stunting before nutrition intervention	22	1826±220a	-, -
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	Total	132	1989±300	
Pyd (nmol/mmol creatinine)				0.006
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NOTE: Mean \pm SD; p < 0.01 for significance of ANOVA; ab p < 0.05 for significance of Duncan

Conclusions

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The Pyd urine of stunted adolescents decreased after being given nutrition intervention and could indicate an improved nutritional status; while the normal adolescents' Pyd urine also decreased and remained in normal nutritional status. This study revealed that Pyd can be used as a sensitive biomarker of linear growth in adolescents.

References

- 1. Hayati AW, Alza Y. Is Urinary Pyridinium Crosslinks Associated with Stunting in Stunting Children in Indonesia. Enviro Research Publishers. 2022;10(1):1-11.
- 2. Gibson RS. Principles of Nutritional Assessment (2nd). New York: Oxford University Press; 2005.
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PAPER FORMAT REVIEW

Paper registration no. : PD060COP

Paper title : Urinary Pyridinium Crosslinks as a Sensitive Biomarker of Linear Growth in

Adolescents

No.	Part of paper	Following author's guidelines?	Suggestion
1	Similarity index	Not yet	Please ensure that: Total similarity index < 25% Individual similarity index < 2%
2	Author Agreement Statement	Yes	Please ensure that: 1. All authors have been listed 2. All authors have signed the form 3. Name of corresponding author is listed
3	Title	Yes	
4	Authors list	No	
5	Affiliations	No	
6	Corresponding author's email	Yes	
7	Summary	Yes	
8	Keywords	Yes	
9	Introduction	Yes	
10	Materials and methods	Yes	
11	Results & discussion	Yes	
12	Conclusion	Yes	
13	References	No	
14	Figures and tables	No	
15	Margins	No	
16	Total number of pages	Yes	

by R07_pd060coo_c1 R07_pd060coo_c1

Submission date: 29-Aug-2022 01:43PM (UTC+0700)

Submission ID: 1888673666

File name: Copy_of_R07_PD060COO_C1.docx (17.59K)

Word count: 1075 Character count: 6436

Summary

Urinary pyridinium crosslinks (Pyd) is a sensitive biomarker of linear growth. This study evaluated the sensitivity of four linear growth indicators: height, body energy, bone mass, and Pyd urine. This study measured linear growth in stunted and normal adolescents before and after nutrition intervention. There was no difference in average results of nutrition interventions on linear growth among groups of adolescents using bone mass and body energy indicators. The change in adolescents' height was not convincing through measuring efficacy of nutrition interventions. The Pyd urine of stunted adolescents before nutrition intervention was significantly different from Pyd urine of normal adolescents.

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References

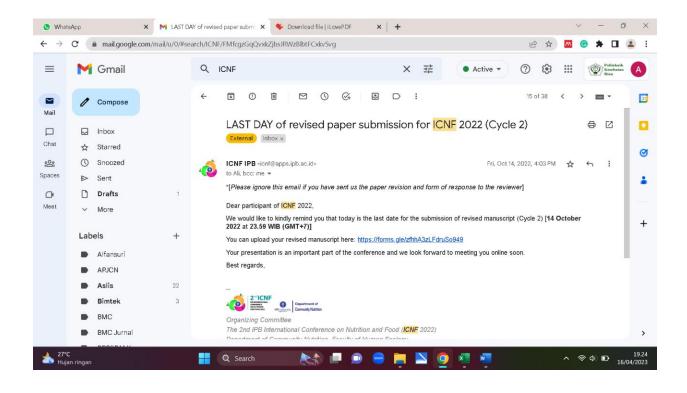
- 1. Hayati AW, Alza Y. Is Urinary Pyridinium Crosslinks Associated with Stunting in Stunting Children in Indonesia. Enviro Research Publishers. 2022;10(1):1-11.
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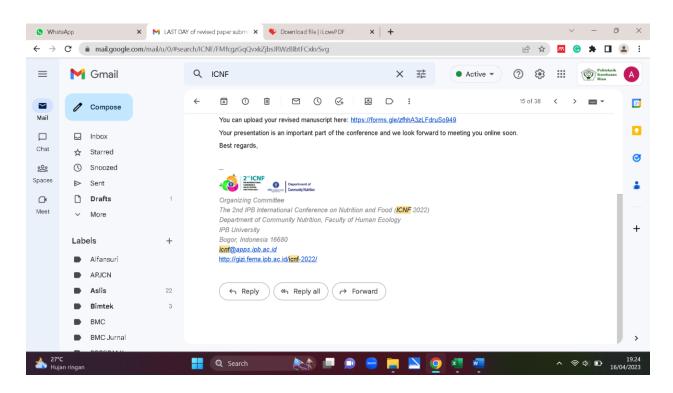
ORIGINALITY REPORT PUBLICATIONS SIMILARITY INDEX INTERNET SOURCES STUDENT PAPERS **PRIMARY SOURCES** www.foodandnutritionjournal.org Internet Source link.springer.com Internet Source Nicole Benzoni, Poonum Korpe, Chrissie Thakwalakwa, Ken Maleta, Kevin Stephenson, Micah Manary, Mark Manary. "Plasma endotoxin core antibody concentration and linear growth are unrelated in rural Malawian children aged 2-5years", BMC Research Notes, 2015 Publication bmcpublichealth.biomedcentral.com **1** % Internet Source Aslis Wirda Hayati, Yessi Alza. "Is Urinary Pyridinium Crosslinks Associated with Stunting in Stunting Children in Indonesia", Current Research in Nutrition and Food Science Journal, 2022

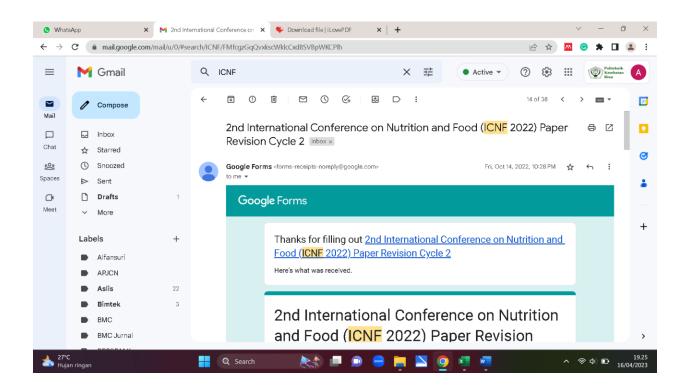
Publication

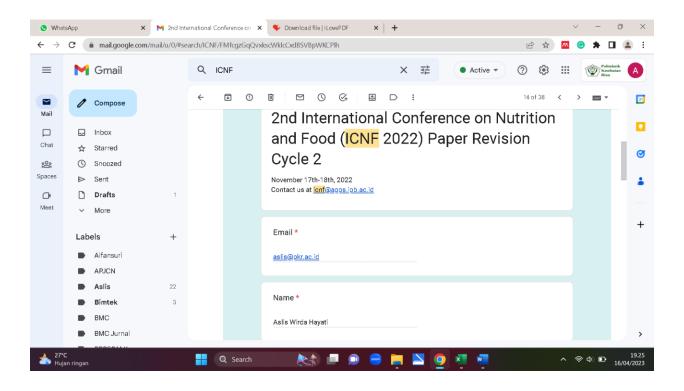
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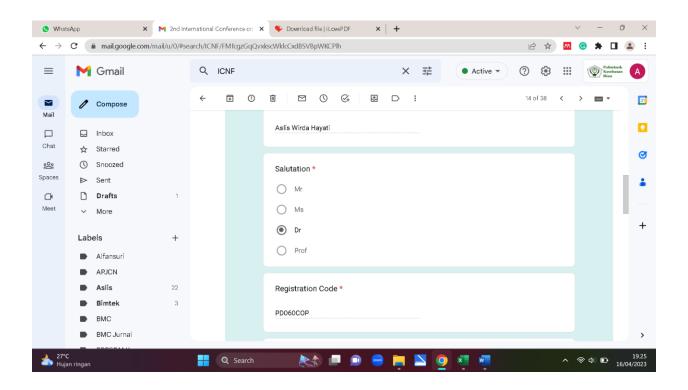
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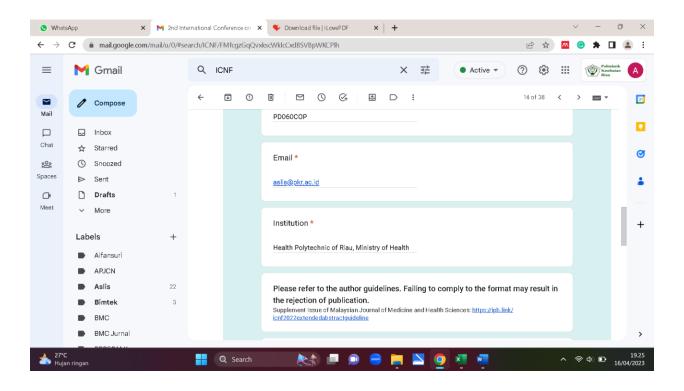


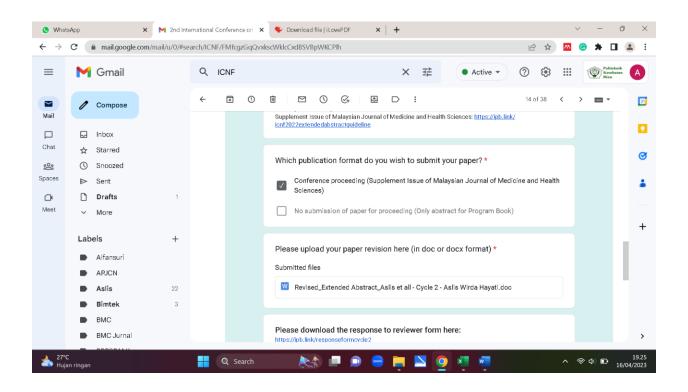


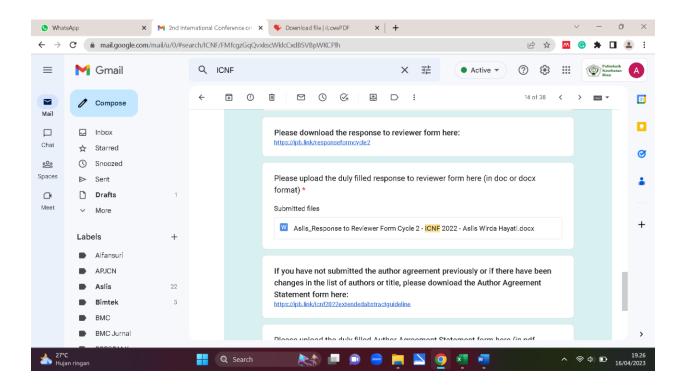


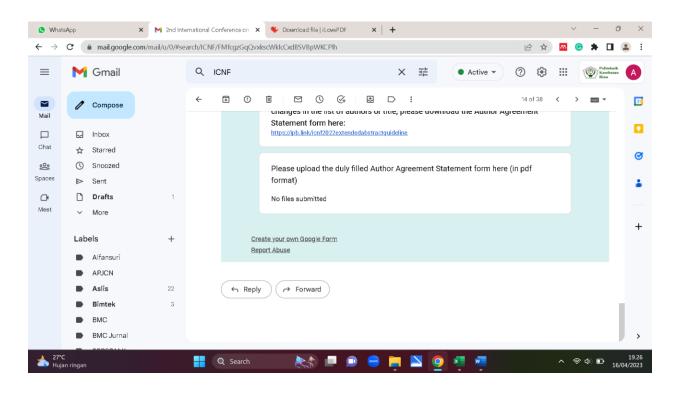


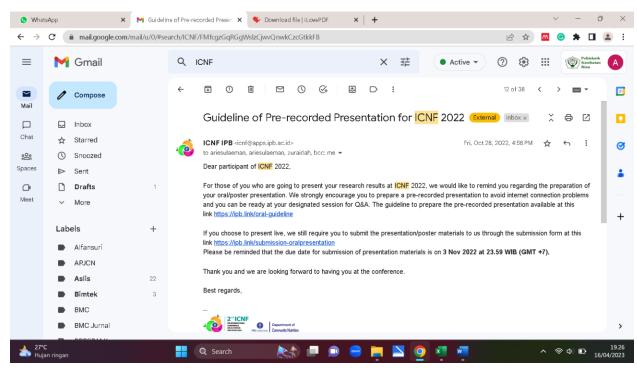


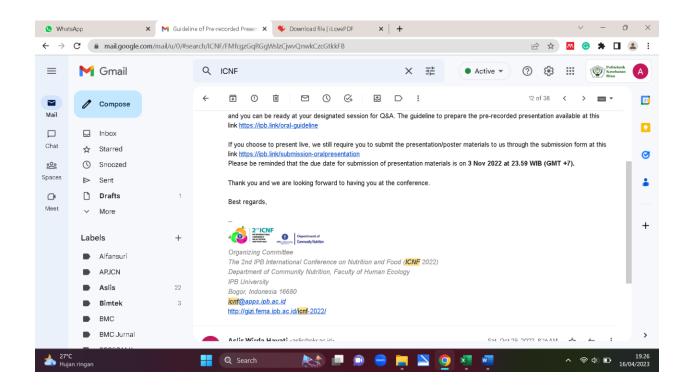


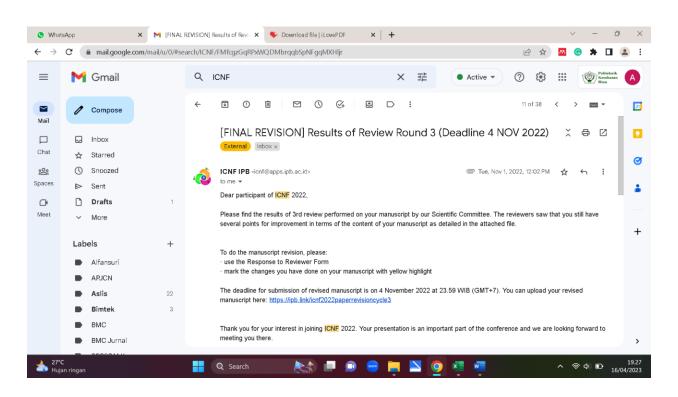


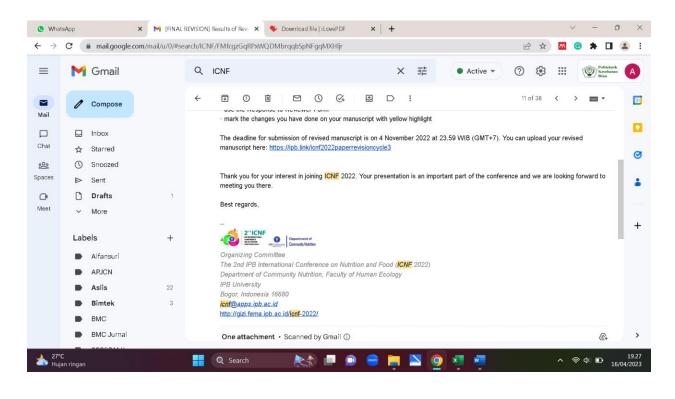


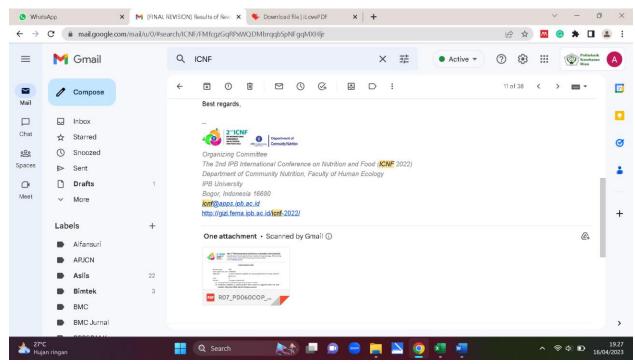














Department of Community Nutrition, Faculty of Human Ecology, IPB University Jl. Lingkar Kampus, Kampus IPB Dramaga, Bogor, Jawa Barat 16680.

Email: icnf@apps.ipb.ac.id

PAPER DECISION FORM

Reviewer code : R07

Paper registration code: PD060COP

Paper title : Urinary Pyridinium Crosslinks as a Convincing Biomarker of Linear Growth in

Adolescents

Cycle : 3

Decision : (reviewer to select one)

a) Full acceptance for publication without any revision in content

b) Conditional acceptance if authors perform minor revision as suggested within one week (deadline: 4 November 2022), with the following comments

No.	Part of paper	Comment/Suggestion
1	Paper title	-
2	 Summary Should be an informative summary of the manuscript. Contains introduction, method, main results, and conclusions. 	The summary is more than 100 words. The value of the AUC should be mentioned.
3	 Keywords Relevant to content and identify the paper's subject, purpose and focus. 	-
4	Introduction - Contains background, research gap, and objectives	Line 41-44: it is stated that the objective is for "early detection of stunting" then why the population of study is adolescent aged 12-15 yo? Stunting could not be corrected properly during adolescent age although it is puberty age where there will be the second growth spurt. The introduction is more than 150 words
5	 Materials and Methods Should provide sufficient detail to allow the work to be reproduced Methods that are already published should be indicated by a reference, and only relevant modifications that are 	It is not clear why the measurement should be twice with two months interval. Since you have decided that it is a diagnostic study with cross-sectional design, there should be only 1 (one) time point of measurement.



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	described	The materials and methods is more than 150
	 Source of material must be given 	words
	 Statistical methods must be specified 	
6a	Results and Discussion	In accordance with the comments in the
	- Results should be clear and presented	method section, there should be revision in
	concisely, using well-designed tables	the narration of the results, table, and figure
	and/or figures	to be only 1 time point.
	- The same data cannot be used in both	,
	styles: table and figure (repetition of data	
	display).	
	 Discussion should explore the significance 	
	of the results of the work and cover the	
	implications and consequences, not only	
	repeating the results	
6b	Tables/ Graphs	In accordance with the comments in the
	- Must contain figure/table title	method section, there should be revision in
	- Should contain figure legends or table	the narration of the results, table, and figure
	notes, if necessary	to be only 1 time point.
	- Appropriate statistical data should be	
	given	
	Canalysians	The ALIC hetween 0.7 to 0.0 is considered
7	Conclusions	The AUC between 0.7 to 0.8 is considered
	- Should not be a summary of the method	acceptable, 0.8 to 0.9 is considered excellent,
	and the study (this is already presented in	and more than 0.9 is considered outstanding.
	the summary).	Therefore, I think the conclusion should not
	- Should identify important outcomes and	directly state that Pyd is better than height.
	their implication for the area of study, or	This sentence in Line 94: "The urinary Pyd is
	recommendations for further research.	better than height measurement to assess
		stunting" should be deleted.
8	Acknowledgements	-
	- Optional	
	- Mention contributions that need to be	
	acknowledged, but do not justify	
	authorship (for example: research	
	funding agencies and individuals who	
	provided help during the research)	
9	List of references	_
	LIST OF FETERICES	

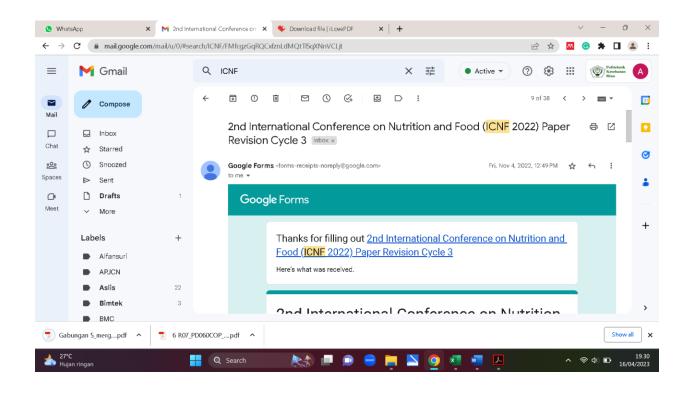


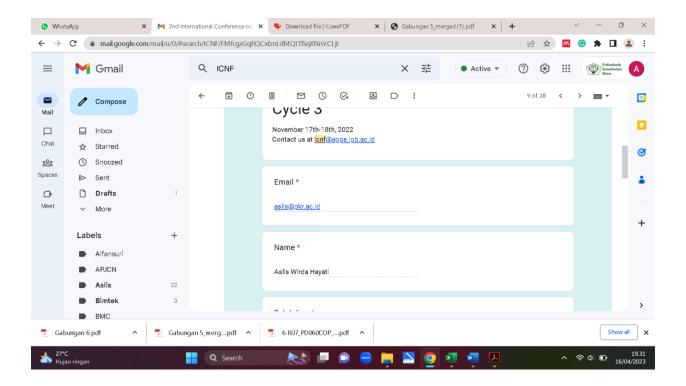
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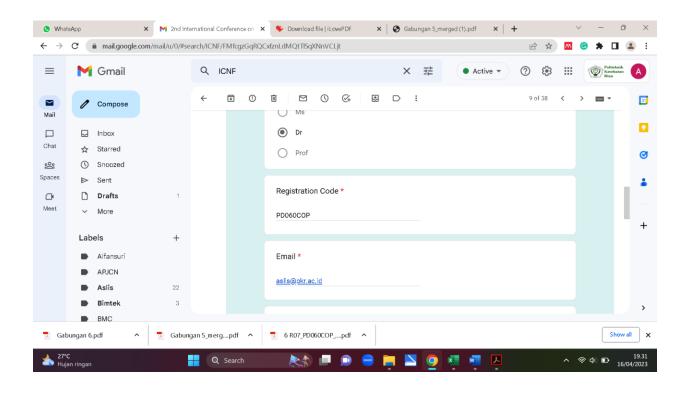
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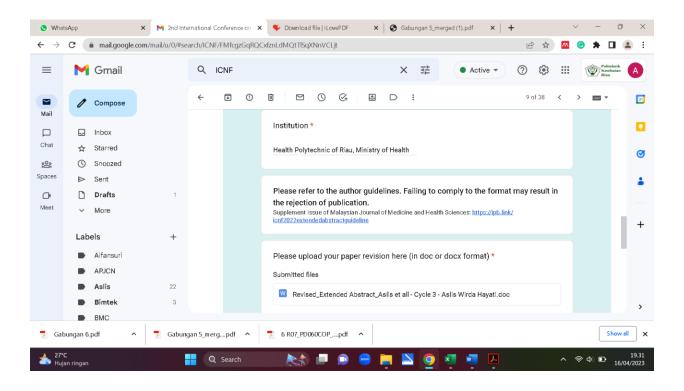
	- Should be relevant to the study	
10	Other aspects	
	Language (filled by reviewer as needed)	

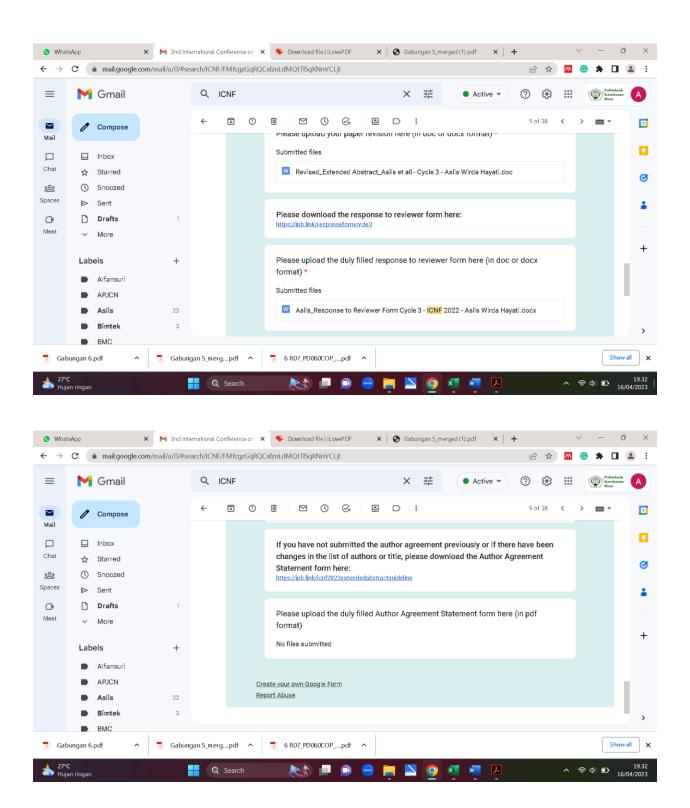
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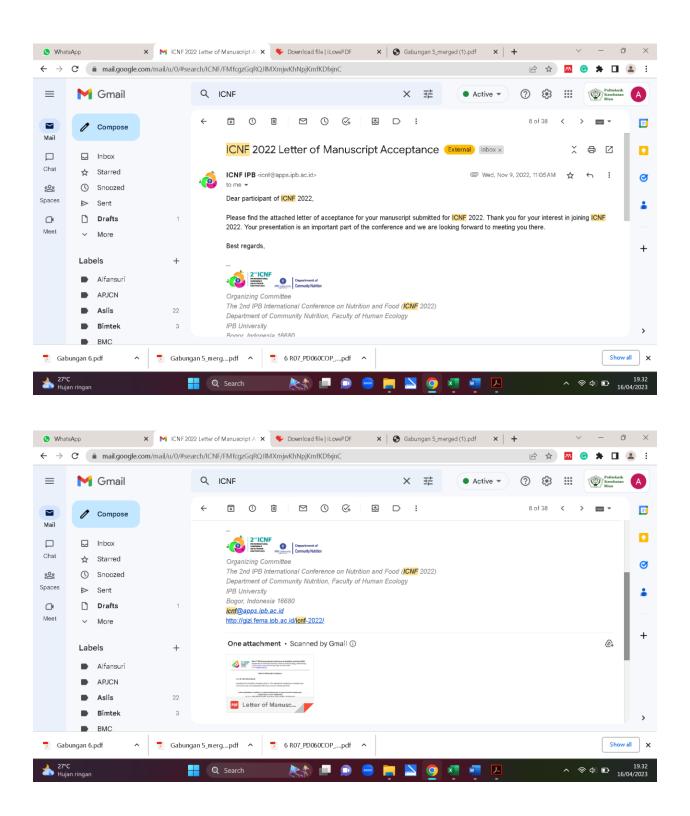














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2	 Summary Should be an informative summary of the manuscript. Contains introduction, method, main results, and conclusions. 	The summary is more than 100 words. The value of the AUC should be mentioned.
3	 Keywords Relevant to content and identify the paper's subject, purpose and focus. 	-
4	Introduction - Contains background, research gap, and objectives	Line 41-44: it is stated that the objective is for "early detection of stunting" then why the population of study is adolescent aged 12-15 yo? Stunting could not be corrected properly during adolescent age although it is puberty age where there will be the second growth spurt. The introduction is more than 150 words
5	 Materials and Methods Should provide sufficient detail to allow the work to be reproduced Methods that are already published should be indicated by a reference, and only relevant modifications that are 	It is not clear why the measurement should be twice with two months interval. Since you have decided that it is a diagnostic study with cross-sectional design, there should be only 1 (one) time point of measurement.



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	described	The materials and methods is more than 150
	 Source of material must be given 	words
	 Statistical methods must be specified 	
6a	Results and Discussion	In accordance with the comments in the
	- Results should be clear and presented	method section, there should be revision in
	concisely, using well-designed tables	the narration of the results, table, and figure
	and/or figures	to be only 1 time point.
	- The same data cannot be used in both	,
	styles: table and figure (repetition of data	
	display).	
	 Discussion should explore the significance 	
	of the results of the work and cover the	
	implications and consequences, not only	
	repeating the results	
6b	Tables/ Graphs	In accordance with the comments in the
	- Must contain figure/table title	method section, there should be revision in
	- Should contain figure legends or table	the narration of the results, table, and figure
	notes, if necessary	to be only 1 time point.
	- Appropriate statistical data should be	
	given	
	Canalysians	The ALIC hetween 0.7 to 0.0 is considered
7	Conclusions	The AUC between 0.7 to 0.8 is considered
	- Should not be a summary of the method	acceptable, 0.8 to 0.9 is considered excellent,
	and the study (this is already presented in	and more than 0.9 is considered outstanding.
	the summary).	Therefore, I think the conclusion should not
	- Should identify important outcomes and	directly state that Pyd is better than height.
	their implication for the area of study, or	This sentence in Line 94: "The urinary Pyd is
	recommendations for further research.	better than height measurement to assess
		stunting" should be deleted.
8	Acknowledgements	-
	- Optional	
	- Mention contributions that need to be	
	acknowledged, but do not justify	
	authorship (for example: research	
	funding agencies and individuals who	
	provided help during the research)	
9	List of references	_
	LIST OF FETERICES	



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	- Should be relevant to the study	
10	Other aspects	
	Language (filled by reviewer as needed)	

Date of review completion: October 28, 2022

