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# The Analysis of Obesogen Phthalates and Genetical Mutation on Teens in Kediri City

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**Abstract:** ***The obesity is an abnormality or disease that with excessive accumulation of body fat tissue. The occurrence of Obesity is caused by many factors, including diet, lifestyle, culture, genetics, and the environment. Fast food, labor-saving equipment, and inactive work habits can make body fat. Obesogen is known as an important element of the cause of obesity. Obesogen is a substance present in the environment, due to the use of certain substances in the processing of foodstuffs and other necessities in meeting human needs, which affects the disturbances of the hormonal system to genetic disorders. There is a difference in levels of obese to phthalates in obese adolescents and not obese. Obesogen phthalate cause obesity in adolescent. The environment influences obesity through genetic disorders through epigenetic DNA methylation. In this study DNA methylation did not occur, but DNA mutations. The conclusion of this study is 1) All obesity and non obesity samples are exposed to phthalate low molecule and high molecule, 2) Phthalate exposure is relatively no different, 3) The junior high school children of Kediri had phthalate molecule low and high phthalate molecule, where the amount of exposure is relatively the same for both obese and non obesity children, men, and women, 4) Genetic changes occur in the form of mutations (not epigenetic methylation), where adolescent obese is obtained 2x from non-obese.***

**Keywords:** Obesity, Obesogen, Tempe, Isoflavones

## 1. Introduction

Obesity is a health problem worldwide, even WHO states that obesity is already a global epidemic, so obesity is a health problem that must be addressed immediately. The contemporary lifestyle that tends to be unbalanced between food intake and physical activity triggers the onset of this incident. The trend of modern society with a lifestyle of stress, competition, good food and excessive, lack of exercise time, triggers the buildup of body fat.

The obesity rests on setting the balance of calories, with reduced intake and increased expenditure followed by maintaining a calorie balance when weight goals have been achieved. The simple idea that obesity can be explained by two factors: energy intake and energy expenditure is a question of lack of success in lowering obesity based on the focus on only these two factors. In animal studies, exposure to environmental chemicals (obesogen) has been shown to increase susceptibility to a number of diseases including obesity. Problems arising from obesity, will interfere with the lives of individuals, including economic losses, including decreased work productivity.

The term of obesogen was invented in year 2006 by Bruce Blumberg, a professor of biology at the University of California, when he discovered that a lead-based compound called organotin may affect laboratory mice gain weight. Obesogen is known as an important element causing obesity. Obesogen is an existing substance in the environment, as a result of the use of certain substances in processing food and other necessities in meeting human needs, which affects the disturbance of the hormonal system to genetic disorders.

The hypothesis that environment and nutrition have an impact on the mechanism of epigenetic gene regulation early in life, and affects metabolism in adults and the vulnerability of chronic diseases (Weaver IC, 2004). Environmental pollutants, the accompanying effects of chemicals present in the scope of everyday life, through the epigenetic process of DNA methylation give genetic changes that cause obesity. This process occurs from the womb and is passed on to the next generation.

## 2. Research Question

The problem of this research is focused on several questions, namely: 1. What is the level of obesogen Phthalate in urine in adolescents? 2. Does obesogen phthalate cause DNA demethylation? 3. Does obesogen phthalate affect increasing obesity in adolescents?

## 3. Literature Review

Obesity is a condition in which the body is overweight due to fat accumulation. Body fat measurements can be performed by measuring the thickness of fat under the skin of the upper arm, waist and abdomen using a skinfold caliper as an anthropometric measurement. Obesity is a condition in which the number and size of fat cells (adyposite cells) increases, while its function changes. Fat cells in addition have excessive energy storage functions, also have a function as a hormone producer and a number of proteins that are important in the physiological functions of the body.

The principle of treating obesity is first to prevent complications and reduce the clinical symptoms that arise due to obesity. The achievement of normal weight is often unrealistic, and should not be a goal of weight loss. Moderate weight loss can provide significant health benefits. Several vitro studies and epidemiological studies suggest a link between exposure to environmental chemistry and

obesity. For example, the risk of obesity is associated with maternal smoking during pregnancy.

Obesogens are foreign chemical compounds that interfere with the normal development and balance of lipid metabolism, which in some cases, can cause obesity. Obesogens are functionally defined as chemicals that improperly alter lipid homeostasis and fat storage, alter set point metabolism, disrupt the energy balance or modify the appetite and satiety settings that lead to fat accumulation and obesity.

Phthalates is a class of multifunctional chemicals used in various consumer care products. Phthalates Highmolecular-weight (eg, di-2-ethylhexyl Phthalate - DEHP - and butylbenzyl Phthalate - BBzP), mainly used as plasticizers in the manufacture of flexible vinyl, which is used in floor and wall cover products, food related goods, and medical equipment. The effect of phthalate on weight gain is related to the activation of peroxisome proliferator-activated receptor γ (PPARγ), antithyroid effects and antiandrogenic effects. PPARγ is the principal regulator of adipogenesis, lipid metabolism, while phthalate provides the potential for adipogenesis. Thyroid disorders are known to play a role in the programming of weight gain in the future. Phthalates are suspected to have anti-androgenic effects, which can cause obesity, because androgens decrease BMI (body mass index).

There are two hormones that have an important role in the regulation of food intake, namely leptin and grelin. Both of these hormones have different pathways to get to the brain, especially the hypothalamus (Klok, 2006). One of the hormones that play a role in the regulation of weight loss is the hormone leptin. These hormones are naturally regulated in controlling the body's normal weight (Galland, 2011).

The Leptin gene (LEP) has been proposed as a candidate gene for thrifty phenotypes because it displays epigenetic variations and is involved in the development of obesity and insulin resistance (Stoger, 2006). LEP is mainly expressed in the differentiation of adipocytes from white fat tissue, and its production, the hormone leptin, has several functions, including regulation of food intake and expression of energy-regulating peptides. Leptin or receptor production defects are strongly associated with obesity (Rankinen, 2005). The leptin hormone is regulated in the metabolism of fat breakdown. Increased leptin hormone will increase the metabolic rate, and the rate of metabolism will decrease if the amount of leptin decreases (Galland, 2011). Leptin requires leptin receptors to react, LEPR. LEPR gene is located on chromosome 1 with 18 exons and 17 introns. The most important and continuously used receptor is the LEP-Rb receptor. These receptors are expressed in the hypothalamus and cerebellum. Besides that, LEP-Rb is also expressed in human vasculature, stomach and placenta.

## 4. Methods

Phthalates are multifunctional chemicals used in various consumer care products. Phthalates Highmolecular-weight (eg, di-2-ethylhexyl Phthalate - DEHP - and butylbenzyl Phthalate -BBzP-). Mainly used as plasticizers in the manufacture of flexible vinyl, which is used in floor and wall cover products, food related goods, and medical equipment.

Exposure to phthalates may come from eating foods and beverages packed in plastic containing phthalates, or inhaling dust in the room with newly installed vinyl miniblinds, wallpaper or floor containing phthalates. Children may be exposed to phthalates by chewing soft vinyl toys or other toy products. Using medical devices such as IV catheter, nasal tube, gastric tube, pharmaceutical products with timed release.

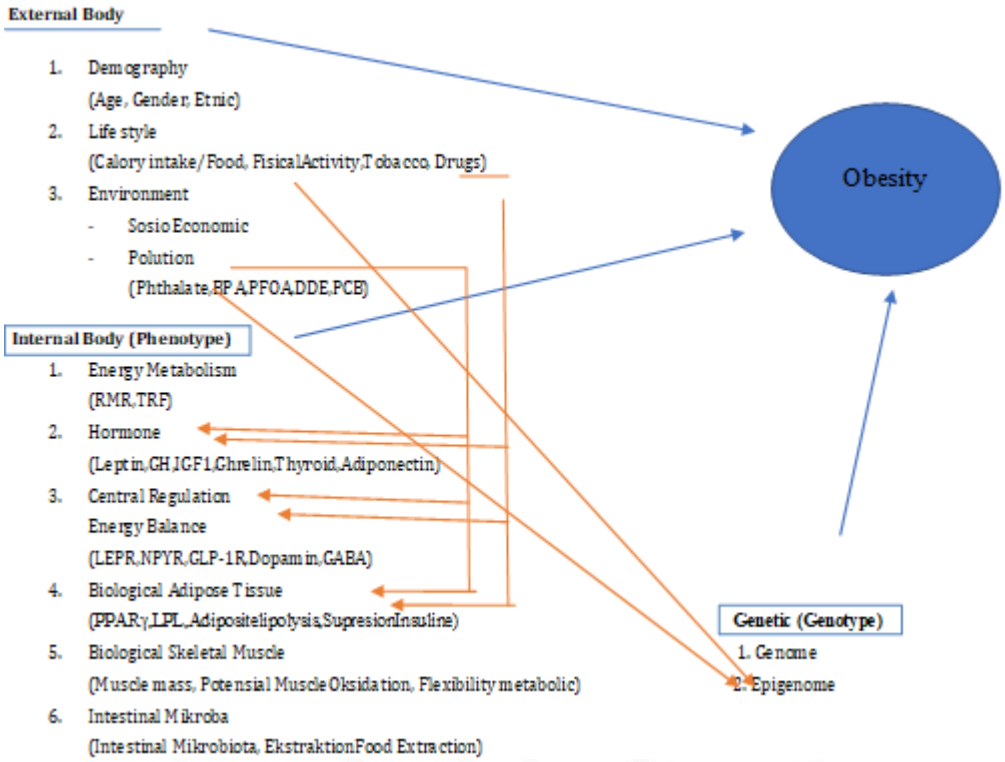


**Figure 1:** Conceptual Framework of Tempe and Obesogen Consumption

## 5. Findings

The obesogen is able to make the size of fat cells in our body getting bigger. The specified sample is 20% of n, with the determination by simple random sampling. The colorimetry method measures the color of a substance as a comparison. Usually white light is used as a light source to compare the absorption of light relative to a substance. Before discussing the demethylation of DNA, the outline will be explained whether DNA methylation. Methylation itself is an event in which the addition of methyl groups to cytosine. This mechanism underlies various transcriptional phenomena, including imprinting, X chromosome inactivation, and transgenerational epigenetic inheritance. DNA demethylation can occur actively by an enzyme with demetilation activity, or passively through multiple replications in the absence of maintenance methyltransferase activity.

Figure 2 show that obesity group average rating is 6.57 with the number 46 ranking. Average ranking group No Obesity is 6.40 by number ranking 32. The amount of Wilcoxon (Wx) = 32 with the value z count -0.081 and probability 0.935 (two-sided test) or 0.4675 for test one side. Because the probability value is 0.4675 more big of α = 0.05, then H0 is accepted, rejects H1. In the SPSS output display shows that average group ranking Obesity consume tempe is 6.40 with a number of 32. Average ranking group No Obesity consuming tempe is 6.57 with number of rank 46. The amount of Wilcoxon (Wx)= 39 with the value of z counts -0.081 and probability 0.935 (two-sided test) or 0.4675 for test one side. Oeh because the probability value is 0.4675 more big of α = 0.05, then H0 is accepted H1 rejected.

Figure 3 shows that the average group ranking for Obesity is 6.71 with the number 47 ranking. Average ranking group No Obesity is 6.20 by number ranking 31. The amount of Wilcoxon (Wx) = 31 with the value of z counts -0.244 and probability 0.808 (two-sided test) or 0.404 for one-sided test. Because the probability value 0.404 is greater from α = 0.05, then H0 is accepted, rejecting H1. In the SPSS output display shows that average group ranking Obesity consume tempe is 5.40 with the number 27. Average ranking group No Obesity consuming tempeh is 7.29 with number of rank 51. The amount of Wilcoxon (Wx) = 27 with the value of z counts -0.895 and probability 0.371 (two-sided test) or 0.1855 for test one side. Because the probability value is 0.1855 more big of α = 0.05, then H0 is accepted H1 rejected.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_MBR_MM_P | 1 | 7 | 6.57 | 46.00 |
| | 3 | 5 | 6.40 | 32.00 |
| | Total | 12 | | |

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_MBR_MM_P | 2 | 5 | 6.40 | 32.00 |
| | 4 | 7 | 6.57 | 46.00 |
| | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate_MBR_MMP |
|---|---|
| Mann-Whitney U | 17.000 |
| Wilcoxon W | 32.000 |
| Z | -.081 |
| Asymp. Sig. (2-tailed) | .935 |
| Exact Sig. [2*(1-tailed Sig.)] | 1.000[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

**Test Statistics[a]**

| | Phthalate_MBR_MMP |
|---|---|
| Mann-Whitney U | 17.000 |
| Wilcoxon W | 32.000 |
| Z | -.081 |
| Asymp. Sig. (2-tailed) | .935 |
| Exact Sig. [2*(1-tailed Sig.)] | 1.000[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

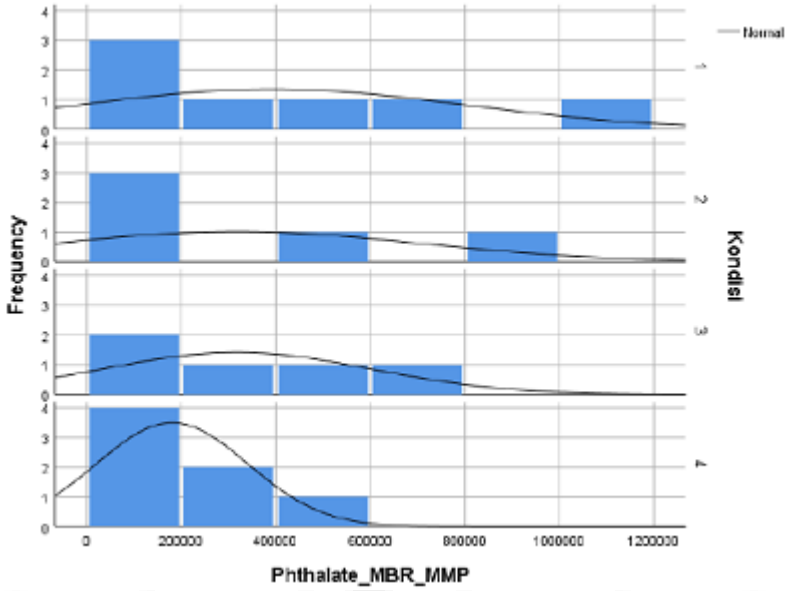


**Figure 2:** The curves show that there is an influence between obesity and not obesity with low molecular weight phthalates, the higher is the low molecular weight MMP phthalate, the higher obesity and vice versa. The higher a person who is obese and not obese consumes tempe, the lower molecular weight MMP phthalate is lower, and vice versa.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_MBR_MEP | 1 | 7 | 6.71 | 47.00 |
| | 3 | 5 | 6.20 | 31.00 |
| | Total | 12 | | |

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_MBR_MEP | 2 | 5 | 5.40 | 27.00 |
| | 4 | 7 | 7.29 | 51.00 |
| | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate_MBR_MEP |
|---|---|
| Mann-Whitney U | 16.000 |
| Wilcoxon W | 31.000 |
| Z | -.244 |
| Asymp. Sig. (2-tailed) | .808 |
| Exact Sig. [2*(1-tailed Sig.)] | .876[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

**Test Statistics[a]**

| | Phthalate_MBR_MEP |
|---|---|
| Mann-Whitney U | 12.000 |
| Wilcoxon W | 27.000 |
| Z | -.895 |
| Asymp. Sig. (2-tailed) | .371 |
| Exact Sig. [2*(1-tailed Sig.)] | .432[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

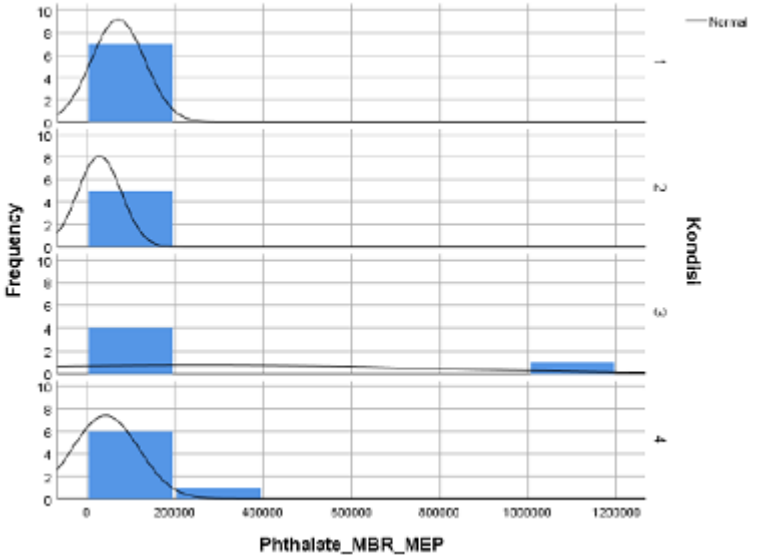


**Figure 3:** The curve shows that there is an influence between obesity and non obese conditions with low molecular weight phthalate MEP, the higher the low molecular weight phthalate MEP is the higher the obesity, and vice versa. The higher is the obese and not obese people consume tempe, the lower molecular weight phthalate of MEP is lower, and vice versa.

Figure 4 shows that Obesity group ranking average is 7.14 with the number 50 ranking. Average ranking group No Obesity is 5.60 by number rank 28. The amount of Wilcoxon (Wx) = 28 with the value z calculate -0.736 and probability 0.462 (two-sided test) or 0.231 for one-sided test. Because the probability value 0.231 is greater from α = 0.05, then H0 is accepted, rejecting H1. In the SPSS output display shows that average group ranking Obesity consume tempe is 6 with a number of 30. The average of ranking group No Obesity consume tempe is 6.86 with amount ranking 48. The amount of Wilcoxon (Wx) = 30 with z count -0.406 and probability 0.685 (test two side) or 0.3425 for test one side. Because the probability 0.3425 more big from α = 0.05, then H0 in accept H1 rejected.

Figure 5 shows that Obesity group ranking average is 6.43 with the number 45 ranking. Average ranking group No Obesity is 6.60 by number ranking 33. The amount of Wilcoxon (Wx) = 45 with the value z count -0.081 and probability 0.935 (two-sided test) or 0.4675 for test one side. Because the probability value is 0.4675 more big of α = 0.05, then H0 is accepted, rejects H1. In the SPSS output display shows that average group ranking Obesity consume tempe is 7 with a ranking of 35. Ratarata ranking group No Obesity consume tempe is 6.14 with amount ranking 43. The amount of Wilcoxon (Wx) = 43 with z count -0.406 and probability 0.685 (test two side) or 0.3425 for test one side. Because the probability 0.3425 more big from α = 0.05, then H0 in accept H1 rejected.

Figure 6 shows that the average group ranking Obesity is 6.14 with the number 43 ranking. Average ranking group No Obesity is 7 by number ranking 35. The amount of Wilcoxon (Wx) = 43 with the number z -0.406 and probability 0.685 (two-sided test) or 0.3425 for test one side. Oeh because the probability value is 0.3425 more big of α = 0.05, then H0 is accepted, rejects H1. In the SPSS output display shows that average group ranking Obesity consume tempe is 6.20 with the number 31. Average ranking group No Obesity consuming tempe is 6.71 with number of rank 47. The amount of Wilcoxon (Wx) = 31 with the value z counts -0.244 and probability 0.808 (two-sided test) or 0.404 for one-sided test. Because the probability value 0.404 is greater from α = 0.05, then H0 is accepted H1 is rejected.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate | 1 | 7 | 7.14 | 50.00 |
| MBR_MiB | 3 | 5 | 5.60 | 28.00 |
| P_MBP | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate_MBR_MiBP_MBP |
|---|---|
| Mann-Whitney U | 13.000 |
| Wilcoxon W | 28.000 |
| Z | -.736 |
| Asymp. Sig. (2-tailed) | .462 |
| Exact Sig. [2*(1-tailed Sig.)] | .530[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate | 2 | 5 | 6.00 | 30.00 |
| MBR_MiB | 4 | 7 | 6.86 | 48.00 |
| P_MBP | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate_MBR_MiBP_MBP |
|---|---|
| Mann-Whitney U | 15.000 |
| Wilcoxon W | 30.000 |
| Z | -.406 |
| Asymp. Sig. (2-tailed) | .685 |
| Exact Sig. [2*(1-tailed Sig.)] | .755[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

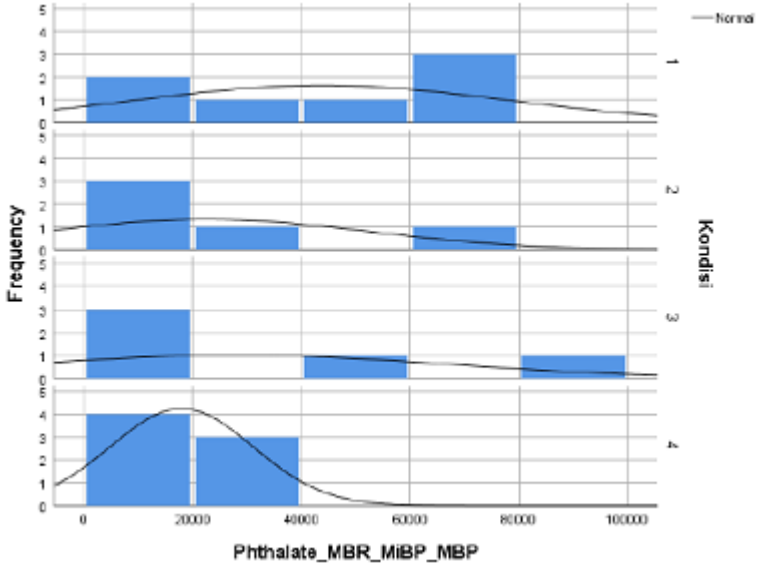


**Figure 4:** The curves show that there is an influence between obesity and non-obesity conditions with low molecular weight phthalate of MiBR and MBP, the higher is the low molecular weight phthalate of the MiBR and MBP of the higher the obesity, and vice versa. The higher is the obese and non-obese individuals consume tempe, the lower molecular weight phthalate of the MiBR and MBP is lower, and vice versa.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate MBT_ME CPP | 1 | 7 | 6.43 | 45.00 |
| | 3 | 5 | 6.60 | 33.00 |
| | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate_MBT_MECPP |
|---|---|
| Mann-Whitney U | 17.000 |
| Wilcoxon W | 45.000 |
| Z | -.081 |
| Asymp. Sig. (2-tailed) | .935 |
| Exact Sig. [2*(1-tailed Sig.)] | 1.000[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate MBT_ME CPP | 2 | 5 | 7.00 | 35.00 |
| | 4 | 7 | 6.14 | 43.00 |
| | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate_MBT_MECPP |
|---|---|
| Mann-Whitney U | 15.000 |
| Wilcoxon W | 43.000 |
| Z | -.406 |
| Asymp. Sig. (2-tailed) | .685 |
| Exact Sig. [2*(1-tailed Sig.)] | .755[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

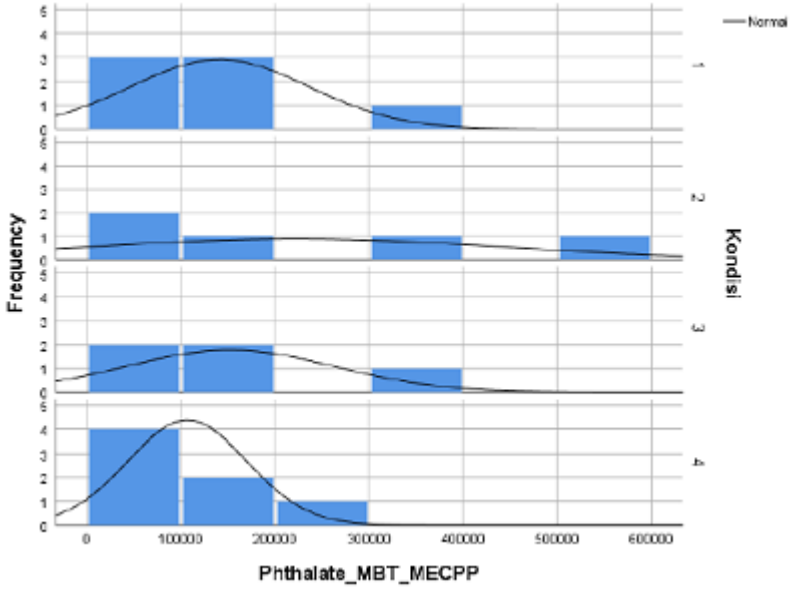

**Figure 5:** The curves show that there is an influence between obesity and non-obese conditions with high molecular weight phthalate MECPP, the higher is the high molecular weight phthalate MECPP, the higher obesity, and vice versa.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_ MBT MC OP | 1 | 7 | 6.14 | 43.00 |
| | 3 | 5 | 7.00 | 35.00 |
| | Total | 12 | | |

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_ MBT MC OP | 2 | 5 | 6.20 | 31.00 |
| | 4 | 7 | 6.71 | 47.00 |
| | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate MBT MCOP |
|---|---|
| Mann-Whitney U | 15.000 |
| Wilcoxon W | 43.000 |
| Z | -.406 |
| Asymp. Sig. (2-tailed) | .685 |
| Exact Sig. [2*(1-tailed Sig.)] | .755[b] |

a. Grouping Variable: Kondisi
b. Not corrected for ties.

**Test Statistics[a]**

| | Phthalate MBT MCOP |
|---|---|
| Mann-Whitney U | 16.000 |
| Wilcoxon W | 31.000 |
| Z | -.244 |
| Asymp. Sig. (2-tailed) | .808 |
| Exact Sig. [2*(1-tailed Sig.)] | .876[b] |

a. Grouping Variable: Kondisi
b. Not corrected for ties.

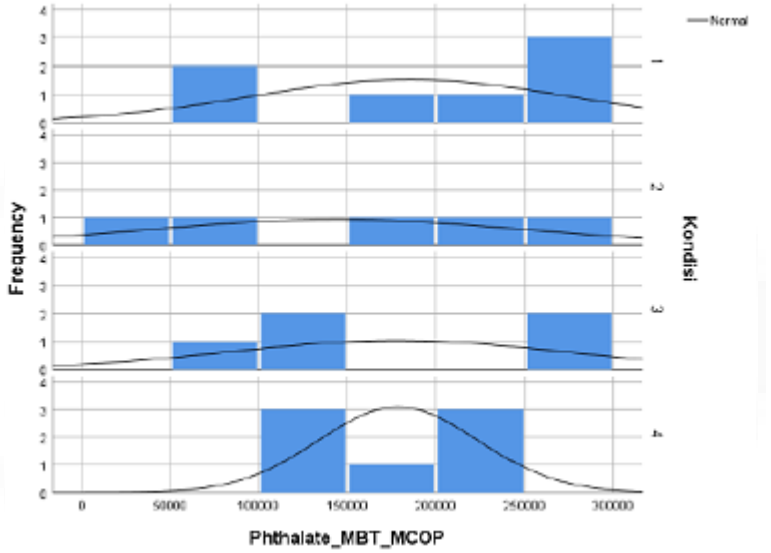


**Figure 6:** The curves show that there is an influence between obesity and non-obesity conditions with high molecular weight phthalate MCOP, the higher of the high molecular weight phthalate MCOPis the higher of the obesity, and vice versa. The higher of the obese and non-obese individuals consume tempe, the higher of molecular weight phthalate of MCOP is lower, and vice versa.

Figure 7 shows that Obesity group ranking average is 7.14 with the number 50 ranking. Average ranking group No Obesity is 5.6 by number rank 28. The amount of Wilcoxon (Wx) = 28 with the value z calculate -0.732 and probability 0.464 (two-sided test) or 0.232 for a one-sided test. Because the probability value of 0.232 is greater from α = 0.05, then H0 is accepted, rejecting H1. In the SPSS output display shows that average group ranking Obesity consume tempe is 6.40 with a number of 32. Average ranking group No Obesity consuming tempe is 6.57 with number of rank 46. The amount of Wilcoxon (Wx) = 32 with the value z calculate -0.081 and probability 0.935 (two-sided test) or 0.4675 for test one side. Because the probability value is 0.4675 more big of α = 0.05, then H0 is accepted H1 rejected.

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_ MBT MC NP | 1 | 7 | 7.14 | 50.00 |
| | 3 | 5 | 5.60 | 28.00 |
| | Total | 12 | | |

**Ranks**

| | Kondisi | N | Mean Rank | Sum of Ranks |
|---|---|---|---|---|
| Phthalate_ MBT MC NP | 2 | 5 | 6.40 | 32.00 |
| | 4 | 7 | 6.57 | 46.00 |
| | Total | 12 | | |

**Test Statistics[a]**

| | Phthalate MBT MCNP |
|---|---|
| Mann-Whitney U | 13.000 |
| Wilcoxon W | 28.000 |
| Z | -.732 |
| Asymp. Sig. (2-tailed) | .464 |
| Exact Sig. [2*(1-tailed Sig.)] | .530[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

**Test Statistics[a]**

| | Phthalate MBT MCNP |
|---|---|
| Mann-Whitney U | 17.000 |
| Wilcoxon W | 32.000 |
| Z | -.081 |
| Asymp. Sig. (2-tailed) | .935 |
| Exact Sig. [2*(1-tailed Sig.)] | 1.000[b] |

a. Grouping Variable: Kondisi

b. Not corrected for ties.

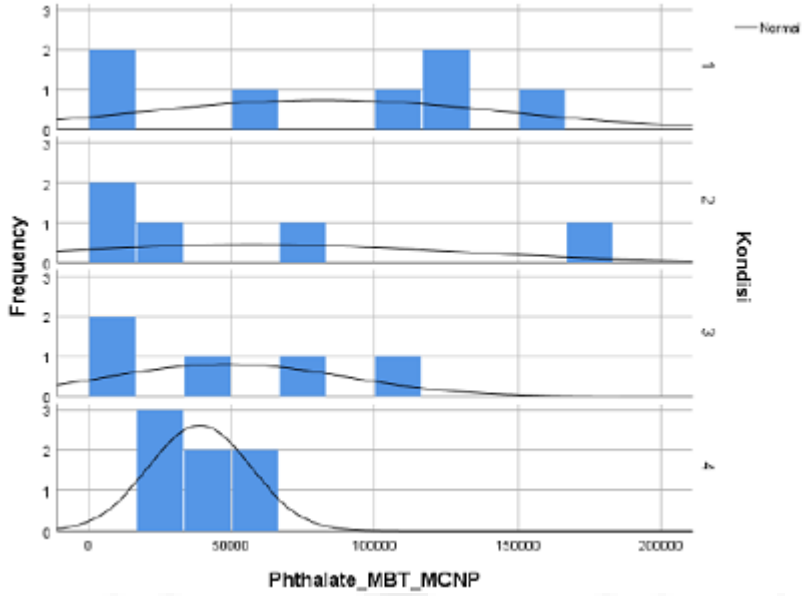


**Figure 7:** The curve that shows that there is an influence between obesity and non-obese conditions with high molecular weight phthalate MCNP, the higher of the phthalate is the high molecular weight MCNP, the higher obesity, and vice versa.

## 6. Conclusion

The conclusion of this study is 1) All obesity and non obesity samples are exposed to phthalate low molecule and high molecule, 2) Phthalate exposure is relatively no different, 3) The junior high school children of Kediri had phthalate molecule low and high phthalate molecule, where the amount of exposure is relatively the same for both obese and non obesity children, men, and women, 4) Genetic changes occur in the form of mutations (not epigenetic methylation), where adolescent obese is obtained 2 times from non-obese.

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