

GAMBARAN KADAR *NITRIC OXIDE* (NO) PADA MASYARAKAT YOGYAKARTA

PROFILE OF *NITRIC OXIDE* (NO) LEVELS IN YOGYAKARTA SOCIETY

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ABSTRAK

Latar Belakang: Senyawa *Nitric Oxide* (NO) merupakan salah satu senyawa penting bagi tubuh. *Nitric oxide* merupakan faktor relaksan untuk pembuluh darah. Dalam jumlah wajar senyawa NO juga memegang peran fisiologis penting pada proses signaling dalam sel dan mengontrol inflamasi, namun dalam jumlah yang berlebihan NO bersifat oksidatif reaktif, genotoksik dan destruktif bagi sel manusia maka dari itu perlu dilakukan penelitian mengenai gambaran kadar NO pada manusia.

Tujuan: Mengetahui kadar NO pada masyarakat Yogyakarta berdasarkan jenis kelamin dan umur.

Metode: Penelitian ini menggunakan desain penelitian cross-sectional. Subjek penelitian berjumlah 44 orang yang terdiri dari 11 laki-laki dan 33 perempuan yang tinggal di Yogyakarta. Sejumlah 44 responden yang telah memenuhi kriteria inklusi dan bersedia mengisi *inform consent* kemudian dilakukan pemeriksaan kadar NO plasma menggunakan metode ELISA. Hasil penelitian akan disajikan dalam bentuk deskriptif dan analisa statistika dengan taraf kepercayaan 95%.

Hasil: Hasil penelitian analisa data berdasarkan jenis kelamin menunjukkan bahwa kadar rata-rata NO pada responden laki-laki lebih tinggi dibandingkan perempuan. Kadar rata-rata NO responden laki-laki yaitu $21,58 \pm \mu\text{mol/L}$ sedangkan responden perempuan yaitu $16,63 \pm \mu\text{mol/L}$. Namun berdasarkan analisa statistik ANOVA didapatkan nilai $p=0,068$ ($p>0,05$) yang berarti tidak terdapat perbedaan yang bermakna antara kadar NO plasma pada laki-laki dan perempuan. Analisa data kadar rata-rata NO berdasarkan umur menunjukkan bahwa responden umur $< 25\text{th}$ lebih rendah dari pada yang berumur $>25\text{th}$. Responden yang berumur $<25\text{th}$ memiliki kadar NO $17,18 \pm \mu\text{mol/L}$ sedangkan yang berumur $>25\text{th}$ yaitu $21,51 \pm \mu\text{mol/L}$. Namun berdasarkan analisa statistik ANOVA didapatkan nilai $p=0,181$ ($p>0,05$) yang berarti tidak terdapat perbedaan yang bermakna antara kadar NO plasma yang berumur $<25\text{th}$ dan $>25\text{th}$.

Kesimpulan: Berdasarkan jenis kelamin kadar rata-rata NO masyarakat Yogyakarta untuk laki-laki yaitu $21,58 \pm \mu\text{mol/L}$ dan perempuan yaitu $16,63 \pm \mu\text{mol/L}$. Berdasarkan umur kadar rata-rata NO masyarakat Yogyakarta untuk berumur $<25\text{th}$ yaitu $17,18 \pm 1,31 \mu\text{mol/L}$ dan $>25\text{th}$ yaitu $21,51 \pm 2,21 \mu\text{mol/L}$.

Kata Kunci: Gambaran, Kadar, *Nitric oxide*

ABSTRACT

Introduction: Nitric Oxide (NO) is one of the important compounds in the body. Nitric oxide is a factor for blood vessel relaxant. In a reasonable amount of NO compounds also controlling an important physiological role in the cell signaling processes and inflammation, however in excessive amounts of NO have a characters as reactive oxidative, genotoxic and destruktif for human cells, therefore necessary to study the profil of NO levels in humans.

Aim: To determine the mean levels of NO in the Yogyakarta society based on gender, age and body mass index (BMI).

Methodology: This study used a cross-sectional study design. The respondents are 44 people consisting of 11 male and 33 female who live in Yogyakarta. A total of 44 respondents who had appropriate the criteria and agree with informed consent then examined the levels of NO plasma using ELISA method. Results of the study will be presented in the descriptive and statistical analysis on the relationship of the levels of NO with gender, age and BMI at 95% confidence level.

Results and Discussion: From this research, the results showed mean levels of NO is 17.87 ± 7.80 $\mu\text{mol/L}$. The results of data analysis by the gender showed mean levels of NO in male respondents is 21.58 ± 8.42 $\mu\text{mol/L}$ and 16.63 ± 7.31 $\mu\text{mol/L}$ in female respondents. The mean levels of NO in male respondents was higher than female. However, there is no significant correlation between mean levels of NO in the male respondents and female based on statistical analysis of independent sample T-test with $p = 0.102$ ($p > 0.05$). The mean levels of NO respondents with aged < 25 years is lower than aged > 25 years. Respondents were aged < 25 years had mean levels of NO is 17.18 ± 8.00 $\mu\text{mol/L}$ while aged > 25 years is 21.5 ± 5.86 $\mu\text{mol/L}$. However, based on statistical analysis with independent sample t-test showed $p = 0.181$ ($p > 0.05$), there is no significant correlation between the mean NO levels aged < 25 years with > 25 years. The test results analysis with independent sample t-test showed no significant correlation between the levels of NO in the non-obese and obese respondents with $p = 0.060$ ($p > 0.05$). Based on the results we know the mean NO levels in non-obese respondents is 16.55 ± 8.09 $\mu\text{mol/L}$, where the obese respondents have mean NO levels is 21.00 ± 6.27 $\mu\text{mol/L}$. From the results of these studies showed the mean levels of NO respondents with obesity is higher than respondents who are non-obese.

Conclusions: The mean NO levels of this research in Yogyakarta society is 17.87 ± 7.80 $\mu\text{mol/L}$. Based on the gender, the mean levels of NO male is 21.58 ± 8.42 $\mu\text{mol/L}$ and 16.63 ± 7.31 $\mu\text{mol/L}$ for female. Based on the age, the mean levels of NO with aged < 25 years is 17.18 ± 8.00 $\mu\text{mol/L}$ and > 25 years is 21.5 ± 5.86 $\mu\text{mol/L}$. Based on the BMI, the mean levels of NO with non-obese is 16.55 ± 8.09 $\mu\text{mol/L}$ and obese is 21.00 ± 6.27 $\mu\text{mol/L}$.

Keywords: Profile, Levels, *Nitric oxide* (NO)

INTRODUCTION

Nitric oxide (NO) is a free radical synthesized by an enzyme Nitric Oxide Synthase (NOS) through a complex reaction. Nitrite Oxide is natural gas in the body was released by endothelial cells and blood vessel dilator substance acts as a short life (Purwadinati *et al.*, 2015). The half-life of NO in the blood vessel is very short (about 3-4 seconds), the examination of NO directly is not easy to do, so the examination with indirect method by using the Griess reaction (Widiastuti, 2010).

In humans, NO is used for several functions intercellular and intracellular signals, such as the transmission of neuronal signals, cytotoxic against pathogens and tumors, cardiac rhythm coordination, and arrangement of cellular respiration activity (JT Groves *et al.*, 2004). Nitric oxide in relation to the blood vessels can cause smooth muscle relaxation, there by functioning as a regulator of flow and blood pressure and prevent platelet aggregation and adhesion. Nitric oxide also helps transport oxygen by dilating the blood vessel walls, thus the transfer of gas to the blood vessel be easy (Idhayu, 2006).

The benefits of NO on the body has been widely studied, one of the most important is its role in the body's immune system. NO cooperate with the lysosomes of macrophages to kill pathogens such as bacteria, fungi and viruses. Nitric oxide help to protect the body from bacteria that enter through the digestive tract. Normal flora that live in the mouth and throat convert nitrate to nitrite in the diet will be changed to NO when exposed to stomach acid. NO this will kill nearly all pathogens ingested with food (Idhayu, 2006).

Nitric oxide if released around the kidney glomerulus, can lead to an increase glomerulus Filtration Rate (GFR). While NO is released by nerve endings in the penis will cause relaxation of the blood vessels so that the corpus cavernosa of the penis fills with blood and produce an erection of the penis (Roitt IM, 2001). The function of NO in reproduction is not only there, NO released by the sperm acrosome can activate the egg in completing phase meiosis II and another phase fertilization. Another benefit of NO on smooth muscle can be seen on the walls of the gastrointestinal tract, NO affects smooth muscle to help peristaltic of the digestive tract. Even NO inhibits smooth muscle

contractions of the uterine wall is very beneficial for mothers with premature babies, so as to maintain the baby to full term (Idhayu, 2006).

Hypertension is still a health problem in the world with an ever-increasing prevalence (AW Dreisbach, 2011). Many risk factors can affect of hypertension in humans such as gender, age, family history, smoking etc. Obesity can lead to hypertension. Obesity increases the risk of hypertension by 2.6 fold in men and 2.2 fold in women (Lilysari O, 2007). Essential hypertension is characterized by endothelial dysfunction and Increased vascular tone and resistance. This is the result of imbalance of endothelium-derived contracting and relaxing factors. Nitric oxide, the which is produced locally by the endothelium is crucial for maintaining vascular tone. It is still unclear whether NO is a marker or a mediator for endothelial dysfunction in hypertension and also whether changes in NO levels occur as primary or secondary events (Saha *et al.*, 2013). So, necessary to study the profil of NO levels in humans.

METHODE

This type of research is descriptive analysis with cross sectional study design. This study was conducted in Yogyakarta. Examination of blood samples carried out in LPPT UGM. Populations are people living in Yogyakarta. Samples are part of a population that is 44 people of Yogyakarta is composed of 11 male and 33 female who had appropriate the criteria which healthy volunteers were evidenced by a health certificate from the hospital authorities, male and female aged 18-60 years and willing to be the subject of (fill informed consent). The independent variable in this study were age, gender and body mass index (BMI), while the dependent variable yiatu NO levels. The research instrument used in this study ELISA Reader is used to measure the levels of NO. Respondents who had appropriate the criteria and agree with informed consent then examined the levels of NO plasma using ELISA method. Results of the study will be presented in the form of descriptive and statistical analysis on the relationship of the levels of NO to gender, age and BMI at 95% confidence level.

RESULTS AND DISCUSSION

Research conducted on the people of Yogyakarta aims to determine how the profile of NO levels in healthy volunteers at Yogyakarta. Respondents were used in this study amounted to 44 people consisting of male and female as many as 11 people as many as 33 people. Age of respondents in this study ranged from 18-60 years consisting of 36 people aged <25 years and 8 people aged >25 years. Characteristics of respondents in this study can be showed in Table 1.

Table 1. Characteristics of Respondents

| Characteristics of Respondents | n | % |
|---------------------------------------|-----------|------------|
| Gender | | |
| Male | 11 | 25 |
| Female | 33 | 75 |
| Total | 44 | 100 |
| Aged | | |
| <25 years | 36 | 81,81 |
| >25 years | 8 | 18,19 |
| Total | 44 | 100 |
| Education | | |
| High School | 10 | 22,73 |
| DIII | 1 | 2,27 |
| S1 | 32 | 72,73 |
| S3 | 1 | 2,27 |
| Total | 44 | 100 |
| Work | | |
| Students | 34 | 77,27 |
| Swasta | 7 | 15,91 |
| Wiraswasta | 3 | 6,82 |
| Total | 44 | 100 |

Nitric Oxide is an important compound in the human body. Many research demonstrate that NO has many benefits such as the immune system can kill the bacteria, vascular homeostasis settings so that interference with the synthesis of NO associated with an increased risk of cardiovascular disease (JT Groves *et al.*, 2004). Nitric Oxide is a natural gas in the body is released by endothelial cells and blood vessel dilator substance acts as a short life with normal levels of 25-45 $\mu\text{mol/L}$ (Purwadinati *et al.*, 2015).

In a reasonable amount of NO compounds also controlling an important physiological role in the cell signaling processes and inflammation, however in excessive amounts of NO have a characters as reactive oxidative, genotoxic and destruktif for human cells (Giordano *et al.*, 2011; Acharya *et al.*, 2010). Excessive NO production can improve the activation of the enzyme guanylate cyclase which may cause negative effects, such as inactivity of certain enzymes, proteins induced stress and even damage DNA (TM Devlin, 2002). From this research, the results showed mean levels of NO is $17.87 \pm 7.80 \mu\text{mol/L}$. Results of the study the levels of NO in Yogyakarta society based on gender can be seen in Table 2.

Table 2. Distribution of NO Levels Based on Gender and Relationship Gender with Levels of NO

| Gender | n | Mean \pm SD of NO Levels ($\mu\text{mol/L}$) | Minumum NO Levels ($\mu\text{mol/L}$) | Maximum NO Levels ($\mu\text{mol/L}$) | p |
|--------|----|--|---|---|-------|
| Male | 11 | 21.58 \pm 8.42 | 8.04 | 36.30 | 0.102 |
| Female | 33 | 16.63 \pm 7.31 | 5.64 | 32.09 | |

Results of the study data analysis by gender showed that mean levels of NO in the male respondents was higher than women. The mean levels of NO in male respondents is $21.58 \pm 8.42 \mu\text{mol/L}$ with minimum NO levels is $8.04 \mu\text{mol/L}$ and the maximum is $36.30 \mu\text{mol/L}$. In the female respondents the mean levels of NO that is $16.63 \pm 7.31 \mu\text{mol/L}$ with minimum NO levels is $5.64 \mu\text{mol/L}$ and a maximum of $32.09 \mu\text{mol/L}$.

Test results analysis with independent sample t-test showed no significant correlation between the mean levels of NO in the male respondents and female with $p = 0.102$. Hypertension is more common in men occurs after the age of 31 years, while in women occurs after age 45 (after menopause). In West Java, the prevalence of hypertension in males approximately 23.1% and approximately 6.5% in women. At the age of 50-59 years the prevalence of hypertension in males approximately 53.8% while the female is about 29% and at the age of 60 years the prevalence of hypertension approximately 64.5%. Isral *et al* (2014) demonstrate the levels of NO in respondents who had hypertension ($26.91 \pm 15.40 \mu\text{mol/L}$) greater than healthy respondents ($25.78 \pm 15. \mu\text{mol/L}$). So, a male can to develop hypertension than female because levels of NO in male is higher than female.

Table 3. Distribution of NO Levels Based on Age and Relationship Age with Levels of NO

| Age (Years) | n | Mean \pm SD of NO Levels ($\mu\text{mol/L}$) | Minumum NO Levels ($\mu\text{mol/L}$) | Maximum NO Levels ($\mu\text{mol/L}$) | p |
|-------------|----|--|---|---|-------|
| <25 | 36 | 17.18 \pm 8.00 | 5.64 | 36.30 | 0.121 |
| >25 | 8 | 21.51 \pm 5.86 | 13.16 | 30.43 | |

Analysis of data the mean levels of NO by age showed that respondents aged <25 years lower than aged >25 years. Respondents were aged <25 years had higher levels of NO $17.18 \pm 5.64 \mu\text{mol/L}$ with minimum NO levels of $5.64 \mu\text{mol/L}$ and a maximum is $36.30 \mu\text{mol/L}$. Respondents were aged >25 years had mean levels of NO is $21.51 \pm 5.86 \mu\text{mol/L}$ with minimum NO levels is $13.16 \mu\text{mol/L}$ and a maximum is $30.43 \mu\text{mol/L}$. The test results analysis with independent sample t-test, the mean levels of NO in respondents aged <25 years and >25 years showed no significant relationship between the mean levels of NO in respondents aged <25 years and >25 years with $p = 0.121$.

Age is a risk factor for hypertension that can not be prevented because according to research by the increasing age of a person, so the greater the risk of developing hypertension. According to Dede Kusmana of the Department of Cardiology, University of Indonesia (2007), that hypertensive

patients aged between 20-30 years, the prevalence is 5-10%, the prevalence of young adults aged between 20-25% and above 50 years of age about 60%. According to Saha *et al* (2013) in the group of respondents with hypertension had higher levels of NO were higher ($43.77 \pm 0.29 \mu\text{mol/L}$) compared to the control group or normotensive ($38.57 \pm 5.02 \mu\text{mol/L}$) which in hypertensive patients Endothelial damage occurs so that the production of NO increases. So that, the increasing age of the higher risk of hypertension that it is influenced by increased levels of NO as a result of endothelial damage.

Table 4. Distribution of NO Levels Based on BMI and Relationship BMI with Levels of NO

| BMI | n | Mean \pm SD of NO Levels ($\mu\text{mol/L}$) | Mininum NO Levels ($\mu\text{mol/L}$) | Maximum NO Levels ($\mu\text{mol/L}$) | p |
|-----------|----|--|---|---|-------|
| Non-Obese | 31 | 16.55 \pm 8.09 | 5.64 | 36.30 | 0.060 |
| Obese | 13 | 21.00 \pm 6.27 | 10.43 | 32.09 | |

Test results analysis with independent sample t-test showed no significant correlation between the mean levels of NO in the non-obese and obese respondents with $p=0.060$. Based on the results, we known mean levels of NO non-obese respondents is $16.55 \pm 8.09 \mu\text{mol/L}$ with minimum levels is $5.64 \mu\text{mol/L}$ and a maximum levels is $36.30 \mu\text{mol/L}$, while the respondents with obesity have mean levels of NO is $21.00 \pm 6,27 \mu\text{mol/L}$ with minimum levels is $10.43 \mu\text{mol/L}$ and maximum levels is $32.09 \mu\text{mol/L}$. From the results of these studies showed the mean levels of NO respondents with higher obesity compared with respondents who are non-obese.

The results were consistent with studies Choi *et al* (2001) which states that NO production is increased in individuals with obesity both in male and female. Choi *et al* (2001) also states that the subcutaneous adipose tissue is a potential source of NO production. In individuals with obesity increased NO production and this increase begins when BMI reaches >25 . Choi *et al* (2001) study shows serum levels of NO on the subject of male and female with a higher excess weight from 4.1 to 4.2 fold compared to subjects that are non-obese. Research Beltowski (2002) also showed increased NO production due to increased production of leptin, which is directly proportional to the increase in adipose tissue. In individuals with obesity decreased bioavailability of NO in circulation caused by impaired synthesis or increased production of NO and Reactive Oxygen Species (ROS). This is related to metabolic factors such as leptin resistance and insulin resistance. On obesity also tend to occur in a condition called oxidative stress-induced inactivation of NO (Lilysari O, 2007; Sulastri D *et al.*, 2010; Fenster CP *et al.*, 2004; Morrison R, 2006; Cahjono H, 2007).

CONCLUSIONS

The mean NO levels of this research in Yogyakarta society is $17.87 \pm 7.80 \mu\text{mol/L}$. Based on the gender, the mean levels of NO male is $21.58 \pm 8.42 \mu\text{mol/L}$ and $16.63 \pm 7.31 \mu\text{mol/L}$ for female. Based on the age, the mean levels of NO with aged <25 years is $17.18 \pm 8.00 \mu\text{mol/L}$ and >25 years is $21.5 \pm 5.86 \mu\text{mol/L}$. Based on the BMI, the mean levels of NO with non-obese is $16.55 \pm 8.09 \mu\text{mol/L}$ and obese is $21.00 \pm 6.27 \mu\text{mol/L}$.

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