

Correlation between Waist Circumference and IGF-1 Levels in an Elderly Population in Bali, Indonesia

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Abstract

Background. Hyperinsulinemia due to insulin resistance is hypothesized to act as a promotor of cancer growth. In addition to the direct effects of hyperinsulinemia on cancer cells, the stimulation of tumor cell growth can also be indirectly mediated through growth factors and receptors such as insulin-like growth factor 1 (IGF-1). Increased cancer risk is also associated with increased adipose tissue, such as in abdominal obesity, due to the higher risk of insulin resistance and hyperinsulinemia. Waist circumference is a parameter that indicates an individual's level of adiposity. In addition, the risk of cancer also increases in the elderly as they age. This study aims to assess the correlation between waist circumference and IGF-1 levels in the elderly population in Bali, Indonesia.

Methodology. This study used a cross-sectional analytical design conducted in the Melinggih Village, Gianyar Regency. The study was conducted in September 2023. This study has been approved by the Research Ethics Commission number 2020/UN14.2.2.VII.14/LT/2023. The study population included elderly individuals residing in the Melinggih Village who were willing to participate. Data analysis encompassed descriptive analysis and the Spearman correlation test.

Result. A total of 88 subjects participated in the study, consisting of 57 females (64.8%) and 31 males (35.2%). A statistically significant but weak correlation coexists between waist circumference and IGF-1 levels.

Conclusion. A weak but statistically significant positive correlation was found between waist circumference and IGF-1 levels in the elderly. However, because of the small sample size, another study with a bigger sample size with enough power to investigate this association needs to be done to validate the results of the current study.

Key words: elderly, IGF-1, waist circumference

INTRODUCTION

Hyperinsulinemia due to insulin resistance is hypothesized to act as a promotor of cancer growth. Moreover, hyperinsulinemia has been implicated etiologically in carcinogenesis. In individuals with long-standing diabetes mellitus (DM), pancreatic beta cells produce endogenous insulin at lower levels than those who are prediabetic. This finding aligns with research indicating a reduced risk of colorectal cancer with a longer duration of DM. A meta-analysis revealed that the risk of colorectal cancer with DM duration less than ten years was 1.3 times, while a duration greater than ten years posed a risk of 1.17 times.¹

In addition to the direct effects of insulin on cancer cells, the promotion of tumor cell growth could also be indirectly mediated through growth factors such as insulin-like growth factor 1 (IGF-1). Elevated insulin concentrations reduce the levels of IGF-binding protein-1, subsequently increasing the amount of bioactive IGF-1. IGF-1 exhibits mitogenic and anti-apoptotic activities and may function as a stimulus for preneoplastic and neoplastic growth. Patients with bladder cancer were also found to have elevated plasma levels of IGF-1.^{2,3}

Beyond the direct effects of insulin, adiposity was also associated with increased cancer risk. Adipose is an

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endocrine-active tissue that produces free fatty acids, interleukin-6 (IL-6), monocyte chemotactic protein, plasminogen activator inhibitor-1 (PAI-1), adiponectin, leptin and tumor necrosis factor- α (TNF- α).^{4,5}

Waist circumference is one parameter indicating an individual's level of adiposity. In the Asian population, waist circumference is also a parameter for the diagnosis of abdominal obesity. In Indonesia, we use body mass index (BMI) as a criterion. A BMI ≥ 23.0 kg/m² is classified as overweight, a BMI between 25 to 29.9 kg/m² is obese grade 1, and a BMI ≥ 30.0 kg/m² is obese grade 2.⁶ Cancer risk also increases in the obese and elderly population. Although abdominal obesity is a protective factor that plays a role in breast tumors in women aged 25 to 64 in Indonesia,⁷ the burden of cancer attributable to obesity is mainly related to digestive organs, with high prevalence in the female population.⁸ Commonly cited cases are colon cancer (23,051), ovarian cancer (21,911) and pancreatic cancer (4,564). A waist circumference (WC) of ≤ 80 cm was linked to a 78% breast cancer risk reduction.⁹ The study aims to examine the correlation between waist circumference and IGF-1 levels in the elderly in Bali, Indonesia.

This research seeks to investigate metabolic disorders, particularly obesity as a component of metabolic diseases, and its relation to cancer risk. It aims to provide data on the relationship between waist circumference and IGF-1 levels in the elderly and its possible role in cancer risk. This research is also expected to serve as a foundation for further studies. Mainly, the objective of this study is to elucidate the correlation between waist circumference and IGF-1 levels in the elderly.

METHODOLOGY

This study employed an analytical cross-sectional research design conducted in Melinggih Village, Gianyar Regency. The research was conducted in September 2023. This study has been approved by the Research Ethics Commission number 2020/UN14.2.2.VII.14/LT/2023. Elderly people (aged 60 and above) from Melinggih Village were invited to participate in this study. Those who provided informed consent, either verbally or in writing, were included. Individuals with a history of malignancy and liver disease were excluded from the research. Consequently, a total sample of 88 individuals was recruited, and their IGF-1 levels were measured using the human Insulin-like Growth Factor-1 ELISA Kit (IGF1) (ab108873) with the double antibody sandwich method produced by Yanaihara Institute Inc. (Multispecies specificity), Cat. No.: RSCYK160R. The examination results were expressed numerically, in ng/mL units.

Descriptive statistics were used to describe the characteristics of the survey respondents. Quantitative data was examined using the Shapiro-Wilk test, while the mean and standard deviation or the median and range were used to summarize the data. Categorical data is described using

frequency and percentage. Spearman's rank correlation was used to determine the correlation between IGF-1 levels and the following: waist circumference, body mass index and waist-hip ratio using the IBM SPSS Statistics version 26.0 program.

RESULTS

Eighty-eight elderly patients from Melinggih Village participated in this study, with a median age of 68.50 years, ranging from 60 to 84. Most participants were female, accounting for 64.8% (n = 57), while males comprised 35.2% (n = 31). Median BMI was 22.50 kg/m² (14.60 to 34.30 kg/m²). It consists of 8.0% (n = 7) underweight, 45.5% (n = 40) normal weight, 13.6% (n = 12) overweight, 26.1% (n = 23) obesity grade 1, 6.8% (n = 6) obesity grade 2.

Meanwhile, the mean waist circumference was 84.50 cm with SD of 10.42 cm overall, with females having an average waist circumference of 84.80 cm (SD = 11.45 cm) and males having an average of 84.16 cm (SD = 8.35 cm). In addition, 61 patients (69.3%) had no central obesity, and 27 patients (30.7%) had central obesity.

Blood pressure readings indicated an average systolic blood pressure of 149.03 mm Hg (SD = 25 mm Hg) and an average diastolic blood pressure of 85.62 mm Hg (SD = 14.99 mm Hg). Mean IGF-1 level of the participants was 4.35 ng/mL (SD = 2.56 ng/mL). The demographic and clinical characteristics of the participants are detailed in Table 1.

There is a statistically significant but weakly positive correlation between the waist circumference and IGF-1 levels (r = 0.255, P = 0.016) (Table 2).

Table 1. Demographic and clinical characteristics of the study participants (N = 88)

Characteristics	Mean \pm SD
Age (years), median (min-max)	68.50 (60 - 84)
Sex, n (%)	
Female	57 (64.8)
Male	31 (35.2)
Height (cm)	152.42 \pm 6.53
BMI (kg/m ²), median (min-max)	22.50 (14.60 - 34.30)
Body weight (kg)	53.20 \pm 10.59
Waist circumference, overall (cm)	84.50 \pm 10.42
Waist circumference, females (cm)	84.80 \pm 11.45
Waist circumference, males (cm)	84.16 \pm 8.35
Systolic blood pressure (mm Hg)	149.03 \pm 25
Diastolic blood pressure (mm Hg)	85.62 \pm 14.99
IGF-1 level (ng/ml)	4.35 \pm 2.56

BMI: Body Mass Index, IGF-1: Insulin Like Growth Factor-1

Table 2. Correlation between select clinical factors and IGF-1 Level

Clinical Factors	r	p-value
Waist circumference and IGF-1	0.255	0.016*
Male	0.366	0.043*
Female	0.222	0.097
Body mass index and IGF-1	0.284	0.007**
Waist-hip ratio and IGF-1	0.062	0.565

*p < 0.05, **p < 0.01, ***p < 0.001

When this correlation was determined by sex, a statistically significant but weakly positive correlation was also found in males ($r = 0.366$, $P = 0.043$), while in females, the correlation was not statistically significant ($r = 0.222$, $P = 0.097$).

The correlation of IGF-1 levels with BMI and waist-hip ratio was also examined. BMI also had a significant weak positive correlation with IGF-1 levels ($r = 0.284$, $P = 0.007$), while its correlation with waist-hip ratio was not statistically significant ($r = 0.062$, $P = 0.565$).

DISCUSSION

Obesity is a chronic disease characterized by a pathophysiological process leading to an increase in adipose tissue mass, consequently increasing morbidity and mortality risk. Numerous conditions facilitate interactions between environmental factors and weight-regulating genes, resulting in a substantial portion of the population having a body mass index (BMI) ≥ 25 kg/m², associated with various metabolic complications of metabolic.¹⁰

The prevalence of obesity has surged in the last three decades, transforming it into a crucial issue that demands particular attention. Obesity is linked to reduced life expectancy and a higher risk of developing type 2 diabetes mellitus (T2DM), cardiovascular diseases and malignancies. Nevertheless, not all individuals with obesity are at high risk of mortality, indicating the existence of a subgroup known as metabolically healthy obese (MHO). MHO individuals do not present with typical metabolic abnormalities like dyslipidaemia, insulin resistance and hypertension. Additionally, there is a subgroup with normal weight but with metabolic abnormalities, termed metabolically obese normal weight (MONW). On the contrary, some individuals with obesity present with one or several metabolic disorders, identified as unhealthy metabolically obese (UMO).¹¹

This study observed a statistically significant positive correlation between waist circumference and IGF-1 levels in the elderly. After we did the subgroup analysis, we also found a statistically significant positive correlation in male patients. We also analyzed BMI and IGF-1 levels, Waist-Hip Ratio and IGF-1 levels and found a statistically significant positive correlation in the former. Increased waist circumference signifies the accumulation of visceral fat, triggering insulin resistance. Insulin resistance gives rise to hyperinsulinemia. Hyperinsulinemia lowers the level of IGF binding protein-1, subsequently increasing levels of bioactive IGF-1. IGF-1 demonstrates mitogenic and anti-apoptotic activities, stimulating preneoplastic and neoplastic growth and forming the basis for elevated cancer risk. Cancer risk rises in the elderly population.¹¹

This aligns with the findings of a meta-analysis by Lin et al. (2020), indicating that individuals with metabolically healthy obesity have a higher risk of cancer compared to those with metabolically healthy non-obesity (OR 1.14;

95% CI 1.05-1.23).¹² Conversely, a meta-analysis conducted by Zheng et al. (2022) found that MHO individuals have a lower cancer risk compared to those with metabolically unhealthy obesity (OR 0.71; 95% CI [0.61,0.84]).¹³

We were unable to analyze other possible confounders affecting IGF-1. We did not examine or measure the insulin resistance (HOMA-IR) due to a lack of resources. However, there are established studies that have reviewed the relationship between WHR and insulin resistance.

This study's limitation arises from the small sample size, which reduces the analytical power. This is also an observational study that cannot prove cause and effect. It is advised to avoid dichotomizing, which eventually reduces power and offers no additional benefits, optimize the power of creating confirmatory experiments centered around important topics and utilize targeted hypothesis testing.

CONCLUSION

A weak but statistically significant positive correlation was found between waist circumference and IGF-1 levels in this elderly population in a village in Bali, Indonesia. However, because of the small sample size, another study with a bigger sample size and enough power to investigate this association needs to be conducted to validate the results of the current study. Based on these research outcomes, the elderly should maintain a healthy lifestyle to prevent an increase in waist circumference as they age.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Credit Author Statement

IMPD: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **WG:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **MRS:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **IMSS:** Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **IBAN:** Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **KS:** Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **AAGB:** Data Curation, Writing – original

draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **PA**: Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **WPP**: Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition.

Author Disclosure

The authors declared no conflict of interest.

Data Availability Statement

Datasets analyzed in the study are under license and not publicly available for sharing.

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