

# ANALYSIS OF REFERENCE RANGE VALUES OF SERUM FOLIC ACID IN INDONESIAN HEALTHY YOUNG ADULT POPULATION

Dewi Nita Restami <sup>1</sup>, Uleng Bahrun <sup>2</sup>, Liong Boy Kurniawan <sup>3\*</sup>,  
Burhanuddin Bahar <sup>4</sup>, Siti Rafiah <sup>5</sup> and Nurahmi <sup>6</sup>

<sup>1</sup> Master of Biomedical Sciences, Hasanuddin University Postgraduate,  
Makassar, South Sulawesi, Indonesia.

<sup>2</sup> Department of Clinical Pathology, Faculty of Medicine,  
Hasanuddin University Makassar, South Sulawesi, Indonesia.

<sup>3</sup> Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University, Makassar,  
South Sulawesi, Indonesia. \*Correspondence Author Email: [liongboykurniawan84@gmail.com](mailto:liongboykurniawan84@gmail.com)

<sup>4</sup> Department of Public Health, Hasanuddin University, Makassar, South Sulawesi, Indonesia.

<sup>5</sup> Department of Anatomy, Faculty of Medicine, Hasanuddin University,  
Makassar, South Sulawesi, Indonesia.

<sup>6</sup> Department of Clinical Pathology, Faculty of Medicine,  
Hasanuddin University Makassar, South Sulawesi, Indonesia.

DOI: [10.5281/zenodo.11466680](https://doi.org/10.5281/zenodo.11466680)

## Abstract

Folic acid or folate is a type of B vitamin. Folic acid is also known as vitamin B9. Folic acid is found in plants such as green vegetables, nuts, seeds, and orange juice. Animal sources of folic acid are mainly in liver and milk. In the body folic acid is activated into Tetrahydrofolate (THF). This study aimed to determine the reference range value of serum folic acid in the Indonesian healthy young adult population. A total of 120 healthy young adult volunteers with an age range of 20 - 40 years consisting of 60 male and 60 female subjects participated in the study. Serum folic acid levels were examined using the (ECLIA) method with a cobas e411 device. Serum folic acid reference range values were determined using percentiles 2.5 - 97.5%. The results showed that the reference range value of serum folic acid in healthy young adults was 4.19 - 19.96 ng/mL, in male subject 4.69 - 20.00 ng/mL and female subjects 3.93 - 18.82 ng/mL. The reference range values of serum folic acid in the Indonesian healthy young adult population are in accordance with the reference ranges reported in other countries.

**Keywords:** Serum Folic Acid, Healthy Young Adults.

## INTRODUCTION

Adulthood is a stage of human development in the age range of 18-65 years, which is divided into young adult development 18-40 years and old adult development 40-65 years. Young adults are in a stage of development characterised by an individual's ability to build close relationships with others. At this stage individuals try to be independent, have a job, build a family, and fulfil their needs. Interaction leads to social relationships, marriage, and having a family as well as being part of society [1].

Young adulthood is a process of human growth and maturity. During this period, unique and continuous changes occur. Physical changes and growth that occur and affect health and nutritional status. One of the common nutritional problems experienced in young adulthood is anaemia. Anaemia is a condition characterised by reduced haemoglobin in the body. Anaemia is characterised by symptoms such as fatigue, dizziness and shortness of breath. Vitamin B9 or folic acid is an essential nutrient in the body. The role of folic acid in the process of protein nucleate synthesis is key to the formation and production of normal red blood cells in the bone marrow [2].

There are risk factors that can increase the vulnerability of health problems at any phase of a person's life. However, it becomes a more detrimental problem if the health is not properly controlled [3]. The most common interactive factor is the combination of excessive dietary energy intake against the background of a fast food environment, lack of physical activity in daily life and genetic susceptibility. Modern food is characterised by readily available snacks, calorific beverages, high-fat foods, high energy density, large portion sizes and relatively low prices [4]. Lack of nutrients and vitamins can cause abnormalities in the body, one of which is folic acid. Folic acid or vitamin B9 can cause megaloblastic anaemia. Data from recent meta-analyses show that folic acid deficiency is associated with hyperhomocysteinemia, hypertension, cardiovascular abnormalities, and cerebrovascular abnormalities as well as an increased risk of cancer events such as breast cancer, pancreatic cancer, and prostate cancer. Moreover, folic acid deficiency is linked to neurological disorders such as decreased cognitive function, dementia, and Alzheimer's disease [5].

Folic acid is one of the vitamins, belonging to the group of B vitamins, is one of the important elements in the synthesis of Deoxyribo Nucleic Acid (DNA). This element is required as a coenzyme in the synthesis of pyrimidine. Folic acid needs can be fulfilled from food consumption such as beef, chicken liver, beef liver, mackerel, crab, spinach, broccoli, beans, strawberries, oranges and wheat but daily food consumption generally cannot fulfil all folic acid needs. Folic acid can be fulfilled with folic acid tablets or folic acid. In addition, folic acid can also prevent DNA changes that can cause cancer. This is the reason why folic acid is recommended to be taken before marriage because folic acid is beneficial to increase fertility and can maintain the health and function of ovarian eggs in women [6].

Folic Acid acts as a coenzyme for several body reactions in the formation of new cells, DNA synthesis as a blue print in cell production, and is necessary for the formation of red blood cells, normal growth and development, maintaining the nervous system, digestive tract, and white blood cells [7]. Symptoms of folic acid deficiency include lethargy, weakness, difficulty breathing, oedema, decreased appetite, depression and nausea. Sometimes glossitis, diarrhoea, and pallor are present and cases of malnutrition are found. On laboratory examination, folic acid deficiency may result in low haemoglobin (Hb), low crista illiaka bone marrow, hyperplastic/megaloblastic bone marrow. In addition, placentation disorders such as abortus habituales, placental abruption, and fetal congenital abnormalities may occur [8].

The need for folic acid in men and women is not differentiated, but depends on age. The need for folic acid per day in infants under one year is 80 µg, in children aged 1-7 years is 160-200 µg, at the age of 7-9 years is 300 µg and at the age of 10 years, adult age is 500 µg and old age is 400 µg. In pregnant women, the need for folic acid per day is 600 µg and in breastfeeding mothers is 500 µg [9]. This study aims to determine the reference range value of serum folic acid in the Indonesian healthy young adult population.

## METHOD

The study was conducted from February to March 2024 at the Clinical Pathology Laboratory, Hasanuddin University Hospital Research Unit (RSUH) and at the Labuang Baji Hospital Clinical Pathology Laboratory, Makassar.

The total sample was 120 healthy young adults aged 20-40 years, consisting of 60 men and 60 women, the inclusion criteria for this study were healthy young adults both male and female aged 18-40 years, the exclusion criteria were pregnant women and currently experiencing infection and inflammation. This study has obtained permission from the Health Research Ethics Committee with ethical approval number 115/UN4.6.4.5.31.1 PP36/2024. Serum folic acid was examined using the (ECLIA) method with a cobas e411 device.

### Data Analysis

Data analysis was performed using licensed statistical software (SPSS version 26). Serum folic acid reference range values were determined by setting limit values between the 2.5% and 97.5% percentiles.

## RESULTS AND DISCUSSION

The study was conducted from February to March 2024 at the Clinical Pathology Laboratory, Research Unit of Hasanuddin University Hospital (RSUH) and at the Clinical Pathology Laboratory of Labuang Baji Hospital, Makassar. The total sample was 120 volunteers who met the inclusion criteria, consisting of 60 men and 60 women (Table 1).

**Table 1: General Characteristics of Research Subjects**

Variables	Mean±SD	Median	Min-Max
Age (20-40 Years) Whole sample	31.72 ± 4.79	32.00	20-40
Male	12.56 ± 4.11	10.15	4-21
Female	10.17 ± 3.71	8.32	4-21

Low serum folic acid is highly variable. These variations most likely reflect differences between study samples in terms of age and health status. Folate deficiency rates are generally considered to be lower but vary between cultures, with frequencies as high as 50% reported in Latin American country populations aged >60 years. The much lower rates of folate deficiency in western countries are thought to reflect differences in nutritional habits and the frequent use of non-prescription vitamin supplements [10].

Table 2. obtained reference range values of serum folic acid in healthy young adult population is 4.19 - 19.97 ng/mL and the average obtained is 10.36 ng/mL, in female sex is 3.93 - 18.83 ng/mL and in male sex is 4.69 - 20.0 ng/mL, the average obtained in female sex is 9.21 ng/mL and male 11.49 ng/mL. Although the male sex is higher than the female. Research by Winkels et al. 2011, found the average of male subjects on folic acid 9.4 ng/mL and women 19.7 ng/mL [11].

The results of Azizah's 2020 study which said that the average intake of folic acid in young adults was 18.0 ug/mL, most respondents did not meet the adequacy of folic acid reaching 94.7% [12]. This may be due to the different daily dietary patterns of men and women. Men tend to consume more food, while women eat less due to the fear of obesity and weight gain.

A study suggests that teenage girls actually skip two meals in favour of snacks. Most snacks are not only devoid of calories, but also contain very few nutrients, and can also interfere with appetite [13].

**Table 2: Reference Range of Folic Acid**

	Gender	N	Mean	SD	Reference Range Percents (2,5-97,5%)
Folic Acid (ng/mL)	Entire Sample	120	10.36	4.07	4.19 – 19.97
	Male	60	1	4.11	4.69 – 20.47
	Female	60	9.21	3.71	3.93 – 18.83

Research by Silvaa, E, A. Hofman states that consumption of folic acid supplements before conception is associated with reduced uteroplacental vascular resistance and reduced hypertension [14].

Table 3 results of folic acid reference range values from various populations in Indonesia and other countries. There are differences in each country. According to Galukande M, et al 2011, reference range values may differ significantly between populations and cultures whose food intake is different [15]. Each laboratory is expected to investigate the transferability of the expected values to its own patient population and if necessary define its own reference range. This study sought to establish folic acid reference values for young adults in Uganda, where the reference range values were found to be 4.17 - 20.0 ng/mL. The results of Wahlin et al. 2015 in Northern Sweden found serum folic acid values of 13.3 - 17.9 ng/mL in serum vitamin B12 and folic acid levels of an adult population aged 35-80 years, folic acid levels with age remained constant throughout the ages studied [16]. In line with research in other countries such as that conducted by Wright et al. 2009 in the UK, the reference value of folic acid was 2.4 - 24.1 ng/mL in the healthy adult population [17], and the study of Pravst et al. 2021 in Europe found folic acid values of 4.3 - 20.4 ng/mL [18], and the results of a study by Pfeiffer et al. 2012 in the United States, found folic acid values of 13.0 - 16.7 ng/mL [19].

The results obtained were a higher prevalence of folic acid in the Aboriginal population but still within normal limits, where 10% of Aboriginal women of childbearing age and most consume store-bought bread so it is likely that they get the benefit of adding to improve nutrition. In line with research conducted in February to March 2024 on serum folic acid in the Indonesian healthy young adult population, found the reference range value of serum folic acid was 4.19 - 19.96 ng/mL. The total sample was 120 volunteers aged 20-40 years, who met the inclusion criteria, consisting of 60 men and 60 women. Serum folic acid reference range values in the Indonesian healthy young adult population are in line with reference ranges reported in other countries [20]. The results of research by Maxwell et al. 2013 in Australia, found folic acid values of 13.5 - 25.0 ng/mL in Aboriginal and non-Aboriginal Western Australian populations aged 16-44 years [21].

**Table 3: Reference Range of Folic Acid in Indonesia and Other Countries**

Reference	Folic acid Reference Range Value
Wahlin et al. 2015 (Swedia Utara)	13.3 – 17.9 ng/mL
Wright et al. 2009 (Inggris)	2.4 – 24.1 ng/mL
Pravst et al. 2021 (Eropa)	4.3 – 20.4 ng/mL
Galukande et al. 2011 (Uganda)	4.17 – 20.0 ng/mL
Pfeiffer et al. 2012 (Amerika Serikat)	13.0 – 16.7 ng/mL
Maxwell et al. 2013 (Australia)	13.5 – 25.0 ng/mL
Restami et al. 2024 (Indonesia, Present Study)	4.19 – 19.96 ng/mL

## CONCLUSIONS

From the results of the above study, it can be concluded that the reference range value of serum folic acid in healthy young adult subjects aged 20 - 40 years is 4.19 - 19.96 ng/mL. The referenge range value of serum folic acid in men, aged 18 - 40 years is 4.69 - 20.0 ng/mL. The raferenge range of serum folic acid in females, aged 18 - 40 years was 3.93 - 18.82 ng/mL.

## Reference

- 1) Pulungan, E. P. dan Zulhaini Sartika A., "Terapi Kelompok Terapeutik Sebagai Upaya Meningkatkan Perkembangan Intimasi Pada Usia Dewasa Muda," *J. Heal. Educ. Lit.*, vol. 5, no. 1, 2022.
- 2) Septa, R. "Hubungan Asupan Vitamin C, Asam Folat Dan Zat Besi Dan Protein Dengan Kadar Haemoglobin Pada Remaja Putri Di Kota Bengkulu," *Svasta Harena Rafflesia*, vol. 2, no. 1, 2023, doi: 10.33088/shr.v2i1.394.
- 3) Samosir, F. J. *Kesehatan Mental Pada Usia Dewasa Dan Lansia (Gambaran Hasil Skrining Kesehatan Mental dengan Kuesioner DASS-42)*. Unpri Press, 2021.
- 4) Sunarto, Nurahmi, Sitti Rafiah, Husain Umar, Liong Boy Kurniawan, U. B. "Analisis Hubungan Indeks Obesitas Dengan Kadar Tumor Necrosis Factor-Alfa Pada Subjek Dewasa Non Diabetes Melitus," *For. Socio Econ. Res. J.*, vol. 16, no. 2, pp. 81–149, 2022.
- 5) Yuandry, R. C. Dewi, and Y. Atifah, S. "Literatur Review : Pengaruh Konsumsi Asam Folat Bagi Ibu Hamil Terhadap Kelahiran Anak Dengan Kelainan Kongenital," pp. 1051–1062, 2023.
- 6) Handayani, S. "Kesehatan Prakonsepsi Dengan Media Leaflet Terhadap Motivasi Catin Program Studi Kebidanan Program Sarjana Pengaruh Edukasi Peran Asam Folat Dalam Kesehatan Prakonsepsi Dengan Media Leaflet Terhadap Motivasi Catin Mengkonsumsi Asam Folat Di UPTD Puskesmas," 2023.
- 7) Sulistyarto, S. "ADLN - Perpustakaan Universitas Airlangga Tesis Pengaruh Pemberian Epinefrin Terhadap ... Yuni Sufyanti Arief," 2016.
- 8) Sandra Gunawan, D. Triwidiyanti, S. and Syafrullah, H. "Hubungan Konsumsi Asam Folat dengan Preeklamsia di RSUD Subang Tahun 2022," *J. Sehat Masada*, vol. 17, no. 1, pp. 39–48, 2023, doi: 10.38037/jsm.v17i1.408.
- 9) Subandrate, Medina Athiah, Ella Amalia, Irsan Saleh, Safyudin, dan Hermansyah, D. R. G. "Peran dalam Metabolisme dan Metode Pemeriksaan," *Maj. Kedokt. Andalas*, vol. 45, no. 1, pp. 51–62, 2022.
- 10) Wahlin, Åke, Lars Bäckman, Johan Hultdin, and Rolf Adolfsson, L.-G. N. "Reference values for serum levels of vitamin B 12 and folic acid in a population-based sample of adults between 35 and 80 years of age," *Public Health Nutr.*, vol. 5, no. 3, pp. 505–11, 2015, doi: doi: 10.1079/phn200167.
- 11) Winkels, I. A. Brouwer, P. Verhoef, F. V. A. Van Oort, J. Durga, R. M. and Katan, M. B. "Gender and body size affect the response of erythrocyte folate to folic acid treatment," *J. Nutr.*, vol. 138, no. 8, pp. 1456–1461, 2011, doi: 10.1093/jn/138.8.1456.
- 12) Azizah, D. I. "Asupan Zat Besi, Asam Folat, dan Vitamin C pada Remaja Putri di Daerah Jatinangor," *J. Kesehat. Vokasional*, vol. 4, no. 4, p. 169, 2020, doi: 10.22146/jkesvo.46425.
- 13) Arif, Y. Fido, Y. dan Fadil Oenzil, "Gambaran Asupan Folat Mahasiswa Fakultas Kedokteran Universitas Andalas," *J. Kesehat. Andalas*, vol. 6, no. 1, p. 181, 2017, doi: doi: 10.25077/jka.v6i1.667.
- 14) Sutrisminah, E. N. "Impact Folic Acid Deficiency on Pregnant Women With," *J. Ilm. Kesehat. Sandi Husada*, vol. 10, pp. 1–13, 2011.
- 15) Galukande, M., J. Jombwe, J. Fualal, R. Baingana, A. G. "Reference values for serum levels of folic acid and Vitamin B12 in a young adult Ugandan population," *Afr. Health Sci.*, vol. 11, no. 2, pp. 240–430, 2011.

- 16) Wright, M. J. King, C. A. Wolfe, H. J. Powers, A. J. A. and Finglas, P. M. "Comparison of (6S)-5-methyltetrahydrofolic acid v. folic acid as the reference folate in longer-term human dietary intervention studies assessing the relative bioavailability of natural food folates: Comparative changes in folate status following a 16-week," *Br. J. Nutr.*, vol. 103, no. 5, pp. 724–729, 2010, doi: 10.1017/S0007114509992339.
- 17) Pravst, Igor, Živa Lavriša, Maša Hribar, Hristo Hristov, Naska Kvarantan, Barbara Koroušič Seljak, Matej Gregorič, Urška Blaznik, Nadan Gregorič, Katja Zaletel, Adrijana Oblak, Joško Osredkar, Katja Žmitek, "Dietary intake of folate and assessment of the folate deficiency prevalence in slovenia using serum biomarkers," *Nutrients*, vol. 13, no. 11, pp. 1–21, 2021, doi: 10.3390/nu13113860.
- 18) Pfeiffer *et al.*, C. M. "Changes in measurement procedure from a radioassay to a microbiologic assay necessitate adjustment of serum and RBC folate concentrations in the U.S. population from the NHANES 1988-2010," *J. Nutr.*, vol. 142, no. 5, pp. 894–900, 2012, doi: 10.3945/jn.111.156901.
- 19) Maxwell *et al.*, S. J. "Baseline investigations of folate status in aboriginal and non-aboriginal West Australians prior to the introduction of mandatory fortification," *Aust. New Zeal. J. Obstet. Gynaecol.*, vol. 53, no. 1, pp. 26–31, 2013, doi: 10.1111/j.1479-828X.2012.01484.x.