

Clinical and Demographic Profiling of Patients with Spondyloarthritis and Its Association with Disease Activity in a Tertiary Hospital in Surabaya, Indonesia

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ABSTRACT

Introduction: The assessment of disease activity is crucial for effectively managing chronic diseases like spondyloarthritis (SpA). Establishing the relationship between disease activity, demographic, and clinical factors is essential for better disease management. This study aimed to delve into the demographic and clinical characteristics of patients at Dr. Soetomo General Academic Hospital, a tertiary hospital in Surabaya, Indonesia, contributing to a comprehensive understanding of SpA occurrences in Surabaya.

Methods: Data were obtained from 38 SpA patients' data classified using ASAS 2009 criteria at Dr. Soetomo General Academic Hospital, excluding individuals with SLE, gout, RA, and septic arthritis. Disease activity was measured using ASDAS-CRP. Association analysis between disease activity, clinical parameters, and demographics was conducted using Mann-Whitney U test and Spearman correlation test.

Results: Results indicated a male-to-female ratio of 8:30, with patients having a median age of 48 (95% CI: 41-53) and most of the patients had a senior high school education (42.11%). The patients exhibited a mean BMI of 25.19 ± 3.77 , a median disease duration of 8.5 (95% CI: 5-10) years, and a median CRP value of 0.2 (95% CI: 0.1-0.5) mg/dL. The majority displayed moderate disease activity, with a median ASDAS-CRP score of 2 (95% CI: 1.5-2.7). Interestingly, no significant correlation was found between disease activity using ASDAS-CRP and the demographic or clinical parameters studied.

Conclusion: Disease activities were found not to have correlations with the demography and clinical parameters of patients with SpA from Dr. Soetomo General Academic Hospital in Surabaya, Indonesia. This emphasizes the necessity for further research to comprehend the intricate relationship between disease activity and diverse influencing factors.

Keywords: Chronic disease; disease activity; patient's demography; spondyloarthritis.

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INTRODUCTION

Spondyloarthritis (SpA) encompasses a spectrum of related conditions that share common clinical features, including inflammatory back pain, peripheral joint involvement, and enthesitis (Dougados and Baeten, 2011). The precise origins and mechanisms behind spondyloarthritis remain uncertain. Nonetheless, multiple strands of evidence suggest that genetics have a significant impact on an individual's vulnerability (Yuliasih et al., 2022). Simultaneous environmental factors, infections and disruptions in gut microbial balance, also play a part in the spondyloarthritis' progressions (Sharip and Kunz, 2020). Numerous investigations have illustrated the involvement of microorganisms in inciting the onset of the condition (Berland et al., 2023; Berthelot et al., 2021).

Disease activity assessment plays a pivotal role in spondyloarthritis treatments. The association between clinical and demographic factors with disease activity is a central aspect of better disease management (Rohde et al., 2017). By investigating how disease activity correlates

with variables such as age, gender, disease duration, and clinical manifestations, the research aimed to identify potential predictive factors that influenced the severity of the condition.

Dr. Soetomo General Academic Hospital, a tertiary hospital in Surabaya, Indonesia, provided a unique clinical setting where patients from diverse demographic backgrounds searched for medical care. Understanding the clinical profiles of these patients is crucial as variations in disease presentation among different demographic groups have been documented in spondyloarthritis (Citera et al., 2021; Malakar et al., 2020; Strand et al., 2013). Thus, analyzing the demographic characteristics of patients visiting this hospital can contribute to a comprehensive understanding of how spondyloarthritis manifests in this population.

The primary objective of this study was to offer comprehensive insights into the demographic and clinical characteristics of patients within a specific hospital



environment, thereby enhancing our understanding of the prevalence and manifestations of this medical condition in Surabaya. By delving into the demographic makeup of the patient population and analyzing their clinical profiles, this research tried to contribute valuable knowledge about the distribution and clinical patterns of the condition in the local context, potentially leading to improved healthcare strategies, targeted interventions, and enhanced patient outcomes.

METHODS

Research design and patients

This study employed a descriptive-analytical research design to investigate the clinical manifestations and levels of Ankylosing Spondylitis Disease Activity Score C-Reactive Protein (ASDAS-CRP) in patients with SpA in order to determine disease activity. The research is conducted at the Rheumatology Polyclinic of Dr. Soetomo General Academic Hospital in Surabaya. The study population consists of patients diagnosed with SpA based on the classification criteria for SpA established by the Assessment of Spondyloarthritis International Society (ASAS) in 2009 (Sieper et al., 2009). The patients were selected from the population of SpA patients in the outpatient installation of Dr. Soetomo General Academic Hospital in Surabaya, based on inclusion and exclusion criteria, using medical records.

Patients' characteristics and data collection methodology

The patients' characteristics such as age, gender, disease duration, and ASDAS-CRP were acquired using medical records as the primary data source for this study. A thorough examination of the patients' medical records facilitated the extraction of pertinent details regarding their demographic and clinical parameters. Furthermore, the patterns of ASDAS-CRP scores were recorded and subjected to analysis to evaluate the extent of disease activity and severity among the patients.

Data Analysis

Demographic and clinical characteristics, including age, sex, and illness duration, were summarized using descriptive statistics. The chosen thresholds for distinguishing these conditions were as follows: less than 1.3 to differentiate between "inactive disease" and "moderate disease activity," less than 2.1 to separate "moderate disease activity" from "high disease activity," and greater than 3.5 to distinguish between "high disease activity" and "very high disease activity". The difference of patients' clinical parameters and the ASDAS-CRP score in sex and education were tested using Mann-Whitney U test. The correlation between ASDAS-CRP score with age, BMI, and disease duration was assessed using Spearman correlation test. All statistical analyses conducted using GraphPad Prism 9 for Windows, were two-tailed, and the statistical significance was established for p-values below 0.05.

RESULTS

Table 1 presents an overview of the demographic attributes of 38 patients with SpA who were treated at Dr. Soetomo General Academic Hospital. The patients' population was predominantly female, with a median age of 48 years. Additionally, a majority of the patients reported completing

their education up to the senior high school level.

Table 1. Patients' demography

Patients' demography	Value
Sex (male:female) [n (%)]	8 (21.05%) : 30 (78.95%)
Age (years) [median (95% CI)]	48 (41-53)
Latest education	
Elementary school [n (%)]	3 (7.89%)
Junior high school [n (%)]	8 (21.05%)
Senior high school [n (%)]	16 (42.11%)
Vocational school [n (%)]	4 (10.53%)
Bachelor [n (%)]	7 (18.42%)

CI: confidence interval

Figure 1 illustrates the clinical parameters of SpA patients at Dr. Soetomo General Hospital, depicting a mean BMI of 25.19 ± 3.77 , a median disease duration of 8.5 years (95% CI: 5-10), a median CRP value of 0.2 (95% CI: 0.1-0.5) mg/dL, and a median ASDAS-CRP score of 2 (95% CI: 1.5-2.7). The majority of patients, comprising 21 individuals, demonstrated an overweight BMI, a distinction that was notably significant when compared to the 16 patients classified as having a normal weight, with only 1 patient falling into the underweight category. Regarding disease duration, a total of 28 patients exhibited a disease duration of ≤ 10 years, revealing a significant distinction from those individuals with disease durations spanning 11-20 years (7 patients) and 21-30 years (3 patients).

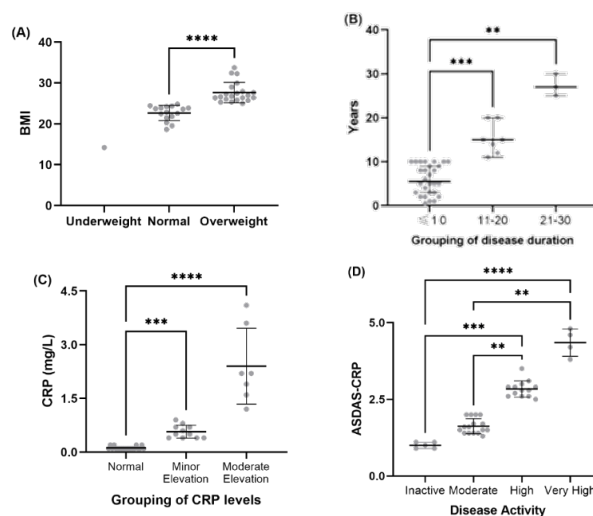


Figure 1. Patients' clinical parameters. (A) BMI. (B) disease duration. (C) CRP levels. (D) ASDAS-CRP. Asterisk indicating a significance using Mann-Whitney test, ** $p < 0.005$, *** $p < 0.0005$, **** $p < 0.0001$

The particular interest was the CRP levels, where a substantial portion of patients demonstrated normal CRP levels (20 patients), significantly different with minor and moderate elevation (11 and 7 patients, respectively), while none of the patients exhibited a high elevation in CRP levels. Disease activity was evaluated using the ASDAS-CRP score, revealing a predominant presence of moderate activity among the 16 patients, which was significantly different with high activity (13 patients) and very high activity (4 patients). The 5 individuals exhibited inactive disease, marking a significant contrast with high and very high activity levels.

Table 2 shows the results of association between ASDAS-CRP with patients' demographic and clinical parameters, but no statistically significant findings are observed across all assessments. The sex and education parameters assessed using the Mann-Whitney U test in conjunction with ASDAS-CRP scores categorized into male and female groups, also elementary school, junior high school, senior high school, vocational school, and bachelor groups for the respective sex and education parameters. Age, BMI, and disease duration were tested with Spearman correlation test.

Table 2. Association between disease activity using ASDAS-CRP and patients' clinical parameters and demography

Parameters	r	p
Sex		0.068
Age	-0.002	0.988
Education		0.822
BMI	0.095	0.570
Disease duration	-0.149	0.371

BMI: body mass index; sex and education parameters assessed using the Mann-Whitney U test; age, BMI, and disease duration tested with Spearman correlation test; no significant found in all parameter tested ($p=0.05$).

DISCUSSION

Initially, SpA was often regarded as primarily affecting males, with ratios as high as 10:1. However, more recent studies have indicated that the difference in sex prevalence is less pronounced (Chimenti et al., 2019, 2021; Kennedy et al., 1993). As shown in our findings, we identified 38 SpA patients, with the majority were female. In our prior research, we also documented a prevalence of females in patients with SpA, where the male-to-female ratio stood at 15:16 (Yuliasih et al., 2023). The SpA typically initiates during the second or third decade of life, onset after the age of 50 reported to be rare. Our result aligned with this pattern, as evidenced by a median patient age of 48 (95% CI: 41-53). A study by Bandinelli et al. (2015) reveals that higher education displays shorter disease durations compared to patients with lower levels of education. In our study, most of patients have completed the higher educations with the highest recorded level being completion of senior high school.

In this study, the patients' BMI predominantly fell within the overweight category. The elevated BMI has been reported to correlate with an increased burden of symptoms and impaired functionality, and reduced treatment responsiveness (Gremese et al., 2014). Overweight may lead to obesity that has the potential to result in persistent biomechanical strain on joints and entheses, a phenomenon that has been shown to constitute a significant risk factor for the onset of SpA in animal models (Bakirci et al., 2019). Other study reveals disease duration emerged as another risk factor for the manifestation of SpA symptoms (Kamo et al., 2014), but in contrast, our study found most of patients had less than 10 years of disease duration. Treatment in patients with early SpA may increase the outcome progression of SpA, also avoid deformities, stiffness, and the development of restrictive respiratory ailments (Wendling et al., 2013).

The CRP level in individuals with SpA is a pivotal marker of inflammation (Landewé et al., 2018), but our finding showed that the most of the patients had normal CRP level. On the other hand, patients diagnosed with SpA who exhibit CRP levels within the normal range could still have active disease based on other clinical indicators (Poddubnyy et al., 2010). A study reveals the overall weak correlation between CRP levels and clinical disease activity in ankylosing spondylitis. Standard CRP tests frequently fail to measure

CRP concentrations by falling below the upper limit of normal, which could be pertinent for evaluating disease activity (Dougados et al., 1999; Landewé et al., 2018).

ASDAS-CRP represent patients' disease activity and plays a key role in prognosis determination (Fatica et al., 2023), and most of the patients included in this study displayed a condition of moderate disease activity. Xu et al. (2011) confirmed ASDAS's effectiveness and its utility in assessing TNF- α inhibitor efficacy in Chinese AS and SpA patients. Monti et al. (2017) stressed the importance of ASDAS-CRP as a strict disease activity index for "treat to target" approaches to prevent inactive disease with fibromyalgia-like symptoms. Yuliasih et al. (2022, 2023) found a correlation between ASDAS-CRP levels and IL-17. Zhang et al. (2022) suggested that ASDAS based on ESR might be superior, and Ramiro et al. (2013) demonstrated ASDAS-CRP's better prediction of radiological changes than BASDAI.

In examining the potential correlations between demography and clinical parameter factors with ASDAS-CRP scores, our analysis revealed that there were no statistically significant associations observed with sex, age, education level, BMI, or disease duration. These findings indicate that within the context of our study, none of these parameters displayed a significant influence on the ASDAS-CRP scores recorded. This suggests that disease activity, as measured by ASDAS-CRP, may not be substantially affected by these demographic and clinical attributes among the patients studied. However, it's important to consider other factors not covered in this study that could have a more pronounced influence on disease activity. For instance, well-established genetic markers like HLA-B27 might play a significant role. Additionally, smoking, which has been linked to aggravated disease activity, and a family history of SpA or related autoimmune conditions, could contribute to higher disease activity. Recognizing this intricate interplay of various genetic, environmental, and lifestyle factors is essential to comprehensively understand disease activity in SpA. Further research is warranted to elucidate the complex relationships among these factors and their combined impact on disease activity.

CONCLUSION

This research provides valuable insights into the demographic and clinical characteristics of patients with SpA in Dr. Soetomo General Academic Hospital in Surabaya and its association with disease activity. The findings indicate the prevalence of female patients, middle-aged individuals, a majority having attained senior high school education, exhibiting overweight BMI, showcasing normal CRP levels, and manifesting moderate disease activity. The absence of correlation between ASDAS-CRP and demographic or clinical parameters signifies a need for further investigation to understand the complex interplay between disease activity and these factors. Future research could explore additional variables, such as genetic markers, lifestyle factors, and patient-specific characteristics, to unravel the underlying mechanisms influencing disease activity in Spondyloarthritis.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

ETHICS CONSIDERATION

Approval for this study was granted by the Ethics Committee of Dr. Soetomo General Academic Hospital for human research under the reference number 2527/125/3/X/2023.

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AUTHOR CONTRIBUTION

Conception and design: CPY, LDR, and YNI. Analysis and interpretation of the data: YNI, Drafting of the article: CPY, LDR, YNI. Critical revision of the article for important intellectual content: LDR, YNI, Y. Administrative, technical, or logistic support: CPY. All authors approved the final version of the manuscript.

REFERENCES

Bakirci S, Dabague J, Eder L, McGonagle D, Aydin SZ. 2019. The role of obesity on inflammation and damage in spondyloarthritis: a systematic literature review on body mass index and imaging. *Clinical and Experimental Rheumatology* 38(1):144–148.

Bandinelli F, Salvadorini G, Sedie AD, Riente L, Bombardieri S, Matucci-Cerinic M. 2015. Impact of gender, work, and clinical presentation on diagnostic delay in Italian patients with primary ankylosing spondylitis. *Clinical Rheumatology* 35(2):473–478. <https://doi.org/10.1007/S10067-015-3005-Z>.

Berland M, Meslier V, Ibraim SM, et al. 2023. Both disease activity and HLA-B27 status are associated with gut microbiome dysbiosis in spondyloarthritis patients. *Arthritis and Rheumatology* 75(1):41–52. <https://doi.org/10.1002/art.42289>.

Berthelot JM, Darrieuort-Laffite C, Trang C, Maugars Y, Le Goff B. 2021. Contribution of mycobiota to the pathogenesis of spondyloarthritis. *Joint Bone Spine* 88(6):105245. <https://doi.org/10.1016/J.JBSPIN.2021.105245>.

Chimenti MS, Alten R, D'Agostino MA, et al. 2021. Sex-associated and gender-associated differences in the diagnosis and management of axial spondyloarthritis: addressing the unmet needs of female patients. *RMD Open* 7(3):e001681–e001681. <https://doi.org/10.1136/RM-DOPEN-2021-001681>.

Chimenti MS, Conigliaro P, Navarini L, Martina FM, et al. 2019. Demographic and clinical differences between ankylosing spondylitis and non-radiographic axial spondyloarthritis: results from a multicentre retrospective study in the Lazio region of Italy. *Clinical and Experimental Rheumatology* 38(1):88–93.

Citera G, Bautista-Molano W, Peláez-Ballestas I, et al. 2021. Prevalence, demographics, and clinical characteristics of Latin American patients with spondyloarthritis. *Advances in Rheumatology* 61(1):1–12. <https://doi.org/10.1186/s42358-020-00161-5>.

Dougados M and Baeten D. 2011. Spondyloarthritis. *The Lancet* 377(9783):2127–2137. [https://doi.org/10.1016/S0140-6736\(11\)60071-8](https://doi.org/10.1016/S0140-6736(11)60071-8).

Dougados M, Gueguen A, Nakache JP, Velicitat P, Zeidler H, et al. 1999. Clinical relevance of C-reactive protein in

axial involvement of ankylosing spondylitis. *The Journal of Rheumatology* 26(4):971–974.

Fatica M, D'Antonio A, Novelli L, et al. 2023. How has molecular biology enhanced our undertaking of axSpA and its management. *Current Rheumatology Reports*, 25(1):12–33. <https://doi.org/10.1007/S11926-022-01092-4>.

Gremese E, Bernardi S, Bonazza S, Nowik M, et al. 2014. Body weight, gender and response to TNF- α blockers in axial spondyloarthritis. *Rheumatology (Oxford, England)*, 53(5):875–881. <https://doi.org/10.1093/RHEUMATOLOGY/KET433>.

Kamo K, Shuto T, Haraguchi A. 2014. Prevalence of spondyloarthritis symptom in inflammatory bowel disease patients: A questionnaire survey. *Modern Rheumatology* 25(3):435–437. <https://doi.org/10.3109/14397595.2014.964925>.

Kennedy LG, Will R, Calin A. 1993. Sex ratio in the spondyloarthropathies and its relationship to phenotypic expression, mode of inheritance and age at onset. *The Journal of Rheumatology* 20(11):1900–1904.

Landewé R, Nurminen T, Davies O, Baeten D. 2018. A single determination of C-reactive protein does not suffice to declare a patient with a diagnosis of axial spondyloarthritis “CRP-negative”. *Arthritis Research & Therapy* 20(1):209–209. <https://doi.org/10.1186/S13075-018-1707-8>.

Malakar A, Kakati S, Barman B, Dutta A. 2020. Clinical presentation and subtypes of spondyloarthritis patients in North East India. *The Egyptian Rheumatologist* 42(4):271–274. <https://doi.org/10.1016/J.EJR.2020.08.003>.

Monti S, Klersy C, Gorla R, et al. 2017. Factors influencing the choice of first- and second-line biologic therapy for the treatment of rheumatoid arthritis: real-life data from the Italian LORHEN Registry. *Clinical Rheumatology* 36(4):753–761. doi: 10.1007/s10067-016-3528-y.

Poddubnyy DA, Rudwaleit M, Listing J, Braun J, Sieper J. 2010. Comparison of a high sensitivity and standard C reactive protein measurement in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis. *Annals of the Rheumatic Diseases* 69(7):1338–1341. <https://doi.org/10.1136/ARD.2009.120139>.

Ramiro S, Tubergen AM, van Heijde D, van der Stolwijk C, et al. 2013. Higher disease activity leads to more damage in the early phases of ankylosing spondylitis: 12-year data from the OASIS cohort. *Arthritis and Rheumatism* 65:S1215–S1216.

Rohde G, Berg KH, Prøven A, Haugeberg G. 2017. The relationship between demographic- and disease-related variables and health-related quality of life in patients with axial spondyloarthritis. *BMC Musculoskeletal Disorders* 18(1). <https://doi.org/10.1186/S12891-017-1693-Z>.

Sharip A and Kunz J. 2020. Understanding the pathogenesis of spondyloarthritis. *Biomolecules* 10(10):1–20. <https://doi.org/10.3390/BIOM10101461>.

Sieper J, Rudwaleit M, Baraliakos X, Brandt J, et al. 2009. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Annals of the Rheumatic Diseases* 68(Suppl 2):ii1–ii44. <https://doi.org/10.1136/ARD.2008.104018>.

Strand V, Rao SA, Shillington AC, Cifaldi MA, et al. 2013. Prevalence of axial spondyloarthritis in united states rheumatology practices: Assessment of spondyloarthritis international society criteria versus rheumatology expert clinical diagnosis. *Arthritis Care and Research* 65(8):1299–1306. <https://doi.org/10.1002/ACR.21994>.

Wendling D, Claudepierre P, Prati C. 2013. Early diagnosis and management are crucial in spondyloarthritis. *Joint Bone Spine* 80(6):582–585. <https://doi.org/10.1016/J.JBSPIN.2013.03.003>.

Xu M, Lin Z, Deng X, et al. 2011. The ankylosing spondylitis disease activity score is a highly discriminatory measure of disease activity and efficacy following tumour necrosis factor- α inhibitor therapies in ankylosing spondylitis and undifferentiated spondyloarthropathies in China. *Rheumatology* 50(8):1466–1472. <https://doi.org/10.1093/rheumatology/ker087>.

Yuliasih, Nisa N, Rahmawati LD, Prastayudha C. 2022. HLA class I and discoveries of the HLA-K (pseudogene) related

to disease severity and progression in patients with spondyloarthritis in Dr. Soetomo General Hospital, a tertiary health care center in Surabaya, Indonesia. *F1000Research* 2022 11:1011. <https://doi.org/10.12688/f1000research.124416.1>

Yuliasih, Permatasari A., Rahmawati LD, Wahyudi MI, Nisa N. 2023. The increasing level of DKK-1 as a new bone formation factor in patients with early spondyloarthritis. *Autoimmune Diseases* 2023. <https://doi.org/10.1155/2023/5543234>.

Zhang S, Peng L, Li Q, Zhao J, et al. 2022. Spectrum of spondyloarthritis among chinese populations. *Current Rheumatology Reports* 24(8):247–258. doi: 10.1007/s11926-022-01079-1.