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The role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in determining the prognosis of patients with testicular cancer (<https://www.balimedicaljournal.org/index.php/bmj/article/view/2977>)

Syah Mirsya Warli, David Ralph Lienhardt Ringoringo, Bungaran Sihombing, Ginanda Putra Siregar, Fauriski Febrian Prapiska

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Bacteriuria in pregnancy in Sanglah Hospital: a descriptive study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3155>)

I Wayan Megadhana, Dewa Gede Sidan Pradnyandita, Putu Doster Mahayasa, I Gusti Ngurah Harry Wijaya Surya

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Risk factors for disability in leprosy patients: a cross-sectional study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3311>)

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ORIGINAL ARTICLE

Increasing dental and oral health knowledge through health promotion of demonstration (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3114>)

Sunanto Sunanto, Erna Handayani

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Predictive factors and the relationship between the early detection of osteoporosis and pathological fractures in Indonesian menopausal women (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3258>)

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Dealing with tests and treatments for HIV, syphilis, and hepatitis B infection to prevent mother-to-child transmission (MTCT) from a tertiary hospital in Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3376>)

Maya Wardiana, Cita Rosita Sigit Prakoeswa, Sawitri Sawitri, Rahmadewi Rahmadewi, Linda Astari, Budi Prasetyo, Budiono Budiono, Afif Nurul Hidayati

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Analysis of Isocitrate Dehydrogenase (IDH) expression in astrocytoma patients: cases of South Sulawesi, Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3078>)

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Absolute Neutrophil Count as Predictor Hematopoietic Recovery in Acute Lymphoblastic Leukemia in Remission Induction Phase Chemotherapy
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Relationship between CD4 levels and mucocutaneous manifestations in HIV-AIDS patients at Dr. Soetomo General Academic Teaching Hospital, Surabaya, Indonesia
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Correlation between sociodemographic and attitude of Malang citizens about self medication on urticaria
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Erna Sulistyowatia, Dewi Martha Indria, Yohanita Nilam Sari

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Factors that influence on Islamic caring behavior
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Comparison of serum and vitreous TGF- β 1 levels in proliferative diabetic retinopathy with and without panretinal photocoagulation laser therapy
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Habibah Setyawati Muhiddin, Rosmiaty Zainal Abidin, Budu ., Junaedi Sirajuddin, Itzar Chaidir Islam, Andi Muhammad Ichsan

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Effects of audio-visual affirmations on toddlers tantrum behavior
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Nanik Handayani, Esty Puji Rahayu

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The effect of metformin on autophagy by LC3 expression in Type 2 Diabetes Mellitus (T2DM) human skeletal muscle cell culture
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Jongky Hendro Prajitno, Agung Pranoto, Robert Dwitama Adiwino, Soebagijo Adi Soelistijo

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Antiproliferation and Apoptosis Effect of Cisplatin and Nanocurcumin on Ovarian Cancer SKOV3 Cell
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Change in ratio levels of KIM-1 / urine creatinine and increase serum creatinine levels in human immunodeficiency virus (HIV) patients receiving tenofovir-based antiretroviral (ARV) combination therapy
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I Dewa Gede Teguh Krisna Murti, I Ketus Agus Somia, I Gde Raka Widiana

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The outcome of hypospadias surgery and it's advanced treatment in Arifin Achmad General Hospital in January 2019 – December 2020
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Evaluating Low Values of Early Diastolic Velocity (e') as a Predictor of Major Cardiovascular Events in Patients with Acute Myocardial Infarction
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The prevalence and characteristics of perineal rupture during vaginal delivery at Sanglah General Hospital and Regional Hospitals in Bali from January 2018 until December 2019 period
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Diphtheria's Outbreak Control in Blitar District
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Gamasiano Alfiansyah, Selvia Juwita Swari, Maya Weka Santi

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Nur Ainiyah, Erika Martining Wardani, Difrano Nobel Bistara, Yurike Septianingrum, Andikawati Fitriyani, Firdaus

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Clinical and radiological profiles of metastatic brain tumor in Indonesia: A study at Dr. Soetomo Hospital, Surabaya
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Nur Akbaryan Anandito, Djohan Ardiansyah

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The effect of workload and length of work on the occurrence of fatigue in workers in the informal industry
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Exploring the role of the combination of propolis and vitamin D3 on VCAM-1 and Caspase-3 expression in preventing atherosclerosis in chronic kidney disease rats
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Darmawan Ismail, Bambang Purwanto, Brian Wasita, Supomo, Ketut Putu Yasa, Soetrisno

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Relationship between plasma adiponectin levels and cellulite
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Combination of diabetic Foot Spa and Sauna Bathing Therapy Decreases the Level of Blood Glucose

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The difference of platelet-white blood cell ratio in severe preeclampsia and normotensive pregnancy
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The effect of Epigallocatechin-3-Gallate (EGCG) combined with low dose sorafenib in apoptosis and Platelet-Derived Growth Factor Receptor (PDGFR) expression in hepatocellular carcinoma rats
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Relationship of age, body mass index (BMI), physical activity, salt intake, and stress with high blood pressure among rural dwellers in Kudat, Sabah
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Mitomycin C, curcumin, and fibrin glue inhibit the cell proliferation and expression of TGF- β in human pterygium fibroblast
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Muhammad Abdurrauf, Ferdian Ramadhan, Nurwasis, Ismi Zuhria, Betty Agustina Tambunan, Hari Basuki Notobroto, Budi Surahman, Evelyn Komaratih

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The clinical pictures of COVID-19 pediatric patients in dr. R. Soedarsono Regional General Hospital, Pasuruan, East Java, Indonesia
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Clinical improvement of patients with moderate-to-severe psoriasis treated with methotrexate at Dr. Soetomo General Hospital, Surabaya, Indonesia
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Features of COVID-19 adult patients and the treatment in Indonesia: a retrospective cohort study
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Dwi Aris Agung Nugrahaningsih, Eko Purnomo, Siswanto, Reviono, Alfi Yasmina, Muh Darwin Prenggono, Nanang Miftah Fajari, Mohammad Rudiandiyah, Harsini, Rul Afiyah Syarif, Eti Nurwening Sholikhah

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The efficacy of probiotics supplementation on the lipid profiles of obese adolescents : a randomized trial
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I Putu Gede Karyana, Ni Luh Sri Apsari, I Wayan Dharma Artana, I Ketut Suarta, Putu Veny Kartika Yantie, Ni Nyoman Metriani Nesa, I Gusti Ngurah Sanjaya Putra, Soetjningsih

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Hematology profile of under five years old children suffered from acute diarrhea at Idaman Banjarbaru Hospital, Indonesia
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Harapan Parlindungan Ringoringo, Jun Rahmawati Surya Mentari, Roselina Panghiyangan, Edi Hartoyo, Rahmiati Lao

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Role of malnutrition inflammation score and interleukin-6 on quality of life of regular hemodialysis patients
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Comparison of effects and differences in duration between exposure to conventional cigarette smoke and electronic cigarette vapors on changes in the number of hippocampal pyknotic pyramidal cell
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The effectiveness of mindfulness based stress reduction and sama vritti pranayama on reducing blood pressure, improving sleep quality and reducing stress levels in the elderly with hypertension
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Iis Noventi, Umdatus Sholihah, Siti Nur Hasina, Lono Wijayanti

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Characteristics of COVID-19 patients with malignancies comorbidity in Sanglah General Hospital, Bali, Indonesia
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Early detection of elevated liver function test in drug-resistant tuberculosis with short term therapy and individual therapy
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Fahmi Dimas Abdul Azis, Hamidah Nurlaila

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The relationship of tumor necrosis factor alpha levels and neutrophils with skin wound age caused by sharp trauma
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M. Husni Cangara, Indah Wulan Sari, Berti Julian Nelwan, Cahyono Kaelan, Gunawan Arsyadi

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Profile of melasma patients in dermatology and venerology outpatient clinic Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3182>)

Apriliin Krista Devi, Budi Utomo, Diah Mira Indramaya, Muhammad Yulianto Listiawan, Sawitri, Dwi Murtiastutik, Cita Rosita Sigit Prakoeswa

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ORIGINAL ARTICLE

Correlation between antenatal magnesium sulfate (MgSO₄) total dose and delivery time interval with umbilical cord blood brain-derived neurotrophic factor (BDNF) levels as a neuroprotection strategy in preterm birth
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2788>)

Muhammad Adrianes Bachnas, Sri Sulistyowati, Uchti Akbar

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Analysis of RGB range value on fingernail image for detecting diabetes mellitus risk

Factors predicting clinical outcome during hospitalization after pericardiocentesis in Sanglah General Hospital, Bali, Indonesia
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Rani Paramitha Iswari Maliawan, I Gede Bagus Bhaskara Wijaksana, I Gusti Ayu Wijayanti Permatasari, Dewa Putu Wisnu Wardhana, Hendy Wirawan, I Gusti Ngurah Putra Gunadhi

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ORIGINAL ARTICLE

The role of revascularization on short-term Heart Rate Variability (HRV) and Signal Averaged Electrocardiogram (SAECG) in Stable Coronary Artery Disease (CAD)
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3147>)

Janry Pangemanan, Agnes Lucia Panda, Victor Giovannie Xaverison Rooroh, Evan Jim Gunawan

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Methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism rather than homocysteine increase the risk of ischemic stroke-associated executive dysfunction
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2503>)

Herpan Syafii Harahap, Muhammad Akbar, Andi Kurnia Bintang, Jumraini Tammasse, Andi Alfian Zainuddin

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(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3096>)

Ima Kurniastuti, Ary Andini, Sabrina Ifahdini Soraya

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ORIGINAL ARTICLE

Self-acceptance of patients that received hemodialysis
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3106>)

Lono Wijayanti, Erika Martining Wardani, Difran Nobel Bistara, Siti Nur Hasina, Iis Noventi

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Ondansetron and metoclopramide: a comparative analysis of effectiveness and cost in hospitalized patients with hyperemesis gravidarum
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3223>)

Lonah, Purwastyastuti, Nafrialdi, Irwinda R, Via Dolorosa Halilintar

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ORIGINAL ARTICLE

User interface design of Be-Health application for children's learning with a gamification approach
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3111>)

Muhammad Wahyudi, Herwanda Ayu Destania, Rochmat Rizky Alfandi, Tri Sagirani

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Development of patient safety learning module based on problem based learning for nursing students at the College of Health Sciences
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3248>)

Ni Nyoman Gunahariati, I Made Sutajaya, Ida Bagus Putu Arnyana, I Gede Sudirtha

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The relationship between diabetes distress and HbA1C level in type 2 diabetes mellitus therapy patients: a systematic review
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2986>)

Zefo Kiyosi Wibowo, Sony Wibisono Mudjanarko, Khairina Khairina

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Bioinformatics assessment on the potential of Lipoteichoic Acid (LTA) of Lactic Acid Bacteria (LAB) as topical therapy for inflammatory skin diseases
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3025>)

Radityastuti, Anang Endaryanto, Ingrid Suryanti Surono, Mohamad Amin, Cita Rosita Sigit Prakoeswa

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ORIGINAL ARTICLE

The effect of antihypertensive monotherapy and combination on blood pressure in stroke patients
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2076>)

Ema Pristi Yunita, Saffana Qolby Mayana, Zamroni Afif

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ORIGINAL ARTICLE

Comparison of prognostic models for severe burn patients in an Indonesian tertiary hospital: retrospective study
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3378>)

Eunice Geraldine Oenarta, Agus Roy Rusly Hariantana Hamid, I Gusti Putu Hendra Sanjaya, I Made Suka Adnyana, Tjokorda Gede Bagus Mahadewa, I Wayan Harimawan Agustinus

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Effect of proteasome inhibitor on serum 8-OHdG and aortic SOD2 in a rat model of atherosclerosis
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3126>)

ismawati ismawati, Ilhami Romus, Mukhyarjon, Jihan Salsabilqis, Nadia Wulandari

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ORIGINAL ARTICLE

Patient preferences for surgery or non-surgery for the treatment of clavus and callus at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3264>)

Arisia Fadila, Iskandar Zulkarnain, Muhammad Yulianto Listiawan, Budi Utomo, Maylita Sari, Irmadita Citrashanty, Bagus Haryo Kusumoputro

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The relationship between catheter placement and the incidence of urinary tract infections in Condong Catur Hospital, Yogyakarta
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3091>)

Kusbaryanto Kusbaryanto, Diana

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ORIGINAL ARTICLE

Soil worms (*Lumbricus rubellus*) as feed additives for piglets' growth, blood profile and immunomodulators
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3190>)

Anak Agung Gde Oka Dharmayudha, Ida Bagus Komang Ardana, Ketut Budiassa, I Made Merdana, I Wayan Nico Fajar Gunawan

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Depot Medroxyprogesterone acetate reduces spermatogonia cells and spermatid cells in the seminiferous tubules of male mice
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Bagus Komang Satriyasa, I Gusti Ayu Widiyanti, I.B.G. Fajar Manuaba

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A structural model of Mapalus culture, health behavior and coronary artery disease incidence in the Minahasa ethnic community in North Sulawesi Province
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2814>)

Jeini Ester Nelwan, Oksfriani Jufri Sumampouw, Adisti Aldegonda Rumayar, Franckie Maramis, Odi Roni Pinontoan, Ester Musa, Jansje Ticoalu, Edi Widjajanto

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A comparison of walking ability between the dynamic hip screw and cephalomedullary nailing fixations in intertrochanteric femur fracture
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3207>)

Karya Triko Biakto, Idrus Andi Paturusi, Harry Supratama Azis, Luky Tandio Putra, Jorvin Kurniawan

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(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3244>)

Sri Andreani Utomo, Abdul Hafid Bajamal, Yuyun Yueniwati Prabowowati Wadjib, Irwan Barlian Immadoel Haq, Vivid Umu Varidha, Dyah Fauziah

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The potential effect of intradermal Botulinum Toxin Type-A (BTA) injection to increase extended random skin flap survival
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3026>)

Caroline Fiona, Iswinarno Doso Saputro, Agus Santoso Budi

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ORIGINAL ARTICLE

Persistence of anti-Salmonella O9 IgM as measured by Tubex® TF may contribute to the over-diagnosis of typhoid fever in endemic areas
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3035>)

I Wayan Adi Pranata, Aly Diana, Marco R Heryanto, Nurhayati Lukman, Herman Kosasih, Hofiya Djauhari, Deni PR Butarbutar, Susana Widjaja, Bachtli Alisjahbana

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ORIGINAL ARTICLE

Seroprevalence SARS-CoV-2 among the academic population of Universitas Gadjah Mada Yogyakarta
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2946>)

Osman Sianipar, Umi Solekhah Intansari, Tri Ratnaningsih, Arum Tri Wahyuningsih, Fuad Anshori, Alfin Harjuno Dwiputro, Adika Zhulhi Arjana

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Early menarche, menstrual duration with dysmenorrhea in adolescents in Surabaya
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3109>)

Nety Mawarda Hatmanti, Yurike Septianingrum, Afita Riah, Firdaus, Ima Nadatien, Siti Maimunah

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The role of apparent diffusion coefficient in differentiating typical from atypical meningioma

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The effect of ACTH4-10Pro8-Gly9-Pro10 on neurotrophin-3 expression in Sprague Dawley rat on acute spinal cord injury
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3143>)

Made Gemma Daniswara Maliawan, Eko Agus Subagio, Budi Utomo, Muhammad Arifin Parenrengi, Asra Al Fauzi, I Ketut Sudiana

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High level of highly sensitivity c-reactive protein levels (hs-CRP) as a risk factor for preterm delivery
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2966>)

Marthin Kolelupun, I Gede Putu Surya, I Nyoman Hariyasa Sanjaya, Tjok Gde Agung Suwardewa, I Wayan Megadhana, I Gede Mega Putra, I Nyoman Gede Budiana, I Wayan Artana Putra

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Retrospective Study on Very Early Relapse of Childhood Acute Lymphoblastic Leukemia at a Reference Centre in Indonesia
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2495>)

Nur Melani Sari, Namira Assyfa Nurazizah, Ronny Lesmana, Nur Suryawan, Susi Susanah

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C-Reactive Protein (CRP)/Albumin Ratio (CAR) pre-treatment as a predictive factor of radiological response after neoadjuvant chemotherapy in Locally Advanced Rectal Cancer (LARC) patients at Dr. Soetomo General Hospital, Surabaya, Indonesia
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3004>)

Fariza Hakim Rio Branco, Tomy Lesmana

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Identification of PST 10 bacterial isolate with α -hemolysis characteristic isolated from pig's tonsil
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3180>)

Hamong Suharsono, I Wayan Suardana, Rizki Kusuma Putri

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ORIGINAL ARTICLE

Characteristic of testicular torsion and predictors of testicular salvage: A retrospective study
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3157>)

Alfryan Janardhana, Besut Daryanto, Budi Suwarno, Arif Rahman Nurdianto

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A novel scoring system to predict postoperative mortality after colorectal cancer surgery: a retrospective cohort study
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2988>)

Anita Hartono, Tomy Lesmana

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Correlation between Urea Creatinine Ratio (UCR) and lipid profile in COVID-19 patients
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2945>)

Indranila Kustarini Samsuria, Ariosta Ariosta, Untung Sujianto

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The variability of temperature, rainfall, humidity and prevalence of dengue fever in Manado City
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2722>)

Odi Roni Pinontoan, Oksfriani Jufri Sumampouw, Jansje Ticoalu, Jeini Ester Nelwan, Ester Cendrawati Musa, Joy Sekeeon

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Clinical presentation of maternal death with COVID-19 in rural tertiary care center: A retrospective-descriptive Study
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3158>)

Devita Kurniawati, Budi Prasetyo, Hanindito Pandu, Arif Rahman Nurdianto

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Aqueous Humour Malondialdehyde Level as Oxidative Stress Marker In Types Of Glaucoma
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2599>)

Maharani Maharani, Puspita Kusuma Dewi, Riski Prihatningtias, Arief Wildan, Trilaksana Nugroho, Edward Kurnia Setiawan Limijadi, Fifin L. Rahmi

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CD44 expression as a potential favorable marker for prognosis in mucoepidermoid carcinoma of salivary gland
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2793>)

Stella Marleen, Lisnawati Rachmadi, Diah Rini Handjari, Kusmardi Kusmardi

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TNF- α serum Level between SARS-CoV-2 Infected Pregnant women with normal pregnant women in RSUD Dr. Soetomo Surabaya
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3377>)

Margaretha Claudhya Febryanna, Manggala Pasca Wardhana, Muhammad Ilham Aldika Akbar, Arif Rahman Nurdianto

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Combination effect of methotrexate with Narrowband Ultraviolet B (NB-UVB) phototherapy in psoriasis vulgaris patients in dermatology and venerology outpatient clinic Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3071>)

Emma Hidayati Sasmito, Iskandar Zulkarnain, Muhammad Yulianto Listiawan, Diah Mira Indramaya, Linda Astari, Budi Utomo, Afif Nurul Hidayati

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Application of Moringa Oleifera leaves extract cream inhibits paw edema in white male Wistar rat (*Rattus norvegicus*) induced by carrageenan 1%
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3384>)

I Gusti Nyoman Darmaputra, I Gusti Ayu Sattwika Pramita, Ketut Kwartantaya Winaya

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Human umbilical cords mesenchymal stem cells for kidney diseases
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3085>)

Dianita Halimah Harahap, Gampo Alam Irdam

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Medical Management of Kidney Stones: a review
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3343>)

Jody Felizio, Widi Atmoko

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REVIEW

Medical education system in Coronavirus Disease 2019 (COVID-19) pandemic: what has been changed from the past era?
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3159>)

Ida Bagus Amertha Putra Manuaba, I Gede Putu Supadmanaba, I Gusti Ayu Sri Darmayani, Dwijo Anargha Sindhughosa, Made Violin Weda Yani

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CASE REPORT

The severe adverse event in a locally anesthetized circumcision: A case report of a breath-holding spell
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3379>)

Syifa Fauziah Fadhly, Irfan Wahyudi, Gerhard Reinaldi Situmorang, Arry Rodjani

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CASE REPORT

Diagnosing and treating Patent Foramen Ovale (PFO) from various manifestations in adults: case series
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2779>)

Todung Donald Aposan Silalahi, Christopher Surya Suwita, Rosaria Oktafiani Darmawan, Benita Rosalie

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Gastrointestinal bleeding as a life-threatening complication of liver abnormality in a Turner syndrome patient
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3259>)

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Uncommon presentation of COVID-19 in ophthalmology: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3006>)

Cisca Kuswidyati, Klarissa Chrisalim, Andre

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CASE REPORT

Profuse haematochezia related to Crohn's disease: a rare case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3204>)

Dilly Niza Paramita, Budi Widodo, Heriyawati Heriyawati

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CASE REPORT

Turner syndrome and tuberculosis in adolescent: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3243>)

Nyoman Titamarita Trisnawan, Florencia Christina Sindhu, Peter Prayogo Hsieh, Arya Putri Ratnasari, Alberto Afrian, Ancelia Limantara, Han's Christian, Made Ratna Dewi, I Wayan Bikin Suryawan

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CASE REPORT

Fatality in a pregnant woman with COVID-19 after a cesarean section: A case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3301>)

Edy Parwanto, Reza Aditya Digambiro, Erdiyan Astato, Assangga Guyansyah

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CASE REPORT

Diagnostic challenges in Waldenström macroglobulinemia: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3160>)

Stella Pravita, Ugroseno Yudho Bintoro, Putu Niken Ayu Amrita

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A single-stage reconstruction on giant scrotal lymphedema: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2907>)

David Ralph Lienhardt Ringoringo, Ramlan Nasution, Kharisma Prasetya Adhyatma

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CASE REPORT

Neonatal varicella: a rare case
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3060>)

Nanda Earlia, Wahyu Lestari, Fitri Dewi Ismida, Annisa Amalia, Aqil Yuliawan Tasrif, Mikyal Bulqiah, Dea Silvia Ramadana

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CASE REPORT

Diagnostic problems and management of pituitary gigantism leading to ischemic stroke and atrial myxoma in young adult patient: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3171>)

Nabilah, Sony Wibisono, Libriansyah, Joni Wahyuhadi, Muhammad Reza Arifianto

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Diagnostic problem on patient with tuberculous colitis mimicking Crohn's disease
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3370>)

Asep Harirohman, Herry Purbayu

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Neurotic excoriation: A case report and literature review
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3195>)

Keiko Yolanda Gunardi, Shannaz Nadia Yusharyahya, Irma Bernadette Sitohang

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CASE REPORT

Advanced MRI prediction of meningioma histopathological classification: a literature review and case presentations
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3100>)

Sri Andreani Utomo, Abdul Hafid Bajamal, Yuyun Yueniwati PW, Irwan Barlian Immaoel Haq, Dyah Fauziah, Eunike Serfina Fajarini

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CASE REPORT

A patient with Type 2 Diabetes Mellitus (T2DM) with Fournier gangrene: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2957>)

Mike Christanti, Jongky Hendro Prajitno, Rio Yudistira Christanto

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CASE REPORT

A severe COVID-19 patient with diabetes mellitus getting dexamethasone with depression disorders: a case report
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/2962>)

Ammar Ammar, Musofa Rusli

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CASE REPORT

The similarity of a desmoid tumor with parasitic leiomyoma: a very rare case report and literature review
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3044>)

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Relationship between CD4 levels and mucocutaneous manifestations in HIV-AIDS patients at Dr. Soetomo General Academic Teaching Hospital, Surabaya, Indonesia



Citra Dwi Harningtyas¹, Damayanti¹, Maylita Sari¹, Muhammad Yulianto Listiawan¹,
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ABSTRACT

Background: CD4 can assess the immune status of a patient with HIV, and this is considered the standard way of assessing and characterizing the severity of HIV-related immunodeficiency. CD4 cell counts are associated with increased mucocutaneous manifestations. This study aims to explain the relationship between CD4 and mucocutaneous manifestations in HIV-AIDS patients.

Methods: This study is analytical with a retrospective cross-sectional design. The data of the present study was obtained from a number of 614 HIV-AIDS patients with mucocutaneous manifestations, but only 149 patients met the inclusion criteria, including the CD4 level data.

Results: The majority of the patients in this study were male (74.5%), which includes patients under the age group of 25-49 years (70.5%). The most common risk factor was heterosexuality (48.3%). Most CD4 levels were in the CD4 group < 200 (64.4%). Based on the distribution of mucocutaneous manifestations, the various cases were reported as infections (55.8%). Pyoderma and syphilis were significantly associated with CD4 counts ≥ 200 cells/mm³ with a risk of 3.7 and 7.8 times than CD4 cells < 200 cells / mm³. On the other hand, candidiasis was higher in CD4 count < 200 cells/mm³ with a significant difference and a risk of 0.3 times compared to CD4 count ≥ 200 cells/mm³.

Conclusion: Several mucocutaneous manifestations can be considered predictors of advanced immunosuppression (low CD4 level), which were pyoderma, syphilis, and candidiasis in this study.

Keywords: AIDS/HIV, CD4, mucocutaneous, immune status.

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INTRODUCTION

Human immunodeficiency virus (HIV) is a retrovirus that attacks and destroys CD4 T lymphocytes (cluster of differentiation 4) and other immune cells with CD4 receptors.^{1,2} Acquired immunodeficiency syndrome (AIDS) is a collection of symptoms or diseases caused by decreased body infection due to HIV and is the final stage of HIV infection.³ The main target of HIV is a subset of lymphocytes originating from the thymus, namely helper T cells, causing deficiency of cellular immunity, which is deficient in T helper lymphocytes (CD4+ cells). The immune status of

children and adults with HIV can be assessed by measuring the absolute (per mm³) or proportion of CD4+ cells, and this is considered the standard way of assessing and characterizing the severity of HIV-related immunodeficiency.^{1,2} Mucocutaneous manifestations were found in 80-95% of HIV-infected patients. Changes in patient status and low CD4 cell counts are associated with an increased frequency of mucocutaneous manifestations. It is because CD4 cells are also present in skin tissue, such as Langerhans cells. Langerhans cells (LCs) are antigen-presenting cells. LC is located

within the epithelium of the skin and mucosa.⁴⁻⁷

Knowledge and awareness of various mucocutaneous manifestations in HIV/AIDS patients are important for doctors because it is very helpful in diagnosing and monitoring the patient's immune status, which is objectively described by CD4 levels. The purpose of this study was to determine the pattern and frequency of mucocutaneous manifestations and their relationship with CD4 levels in HIV/AIDS patients. This analytical study aims to explain the relationship between CD4 and mucocutaneous manifestations in

HIV-AIDS patients at UPIPI RSUD Dr. Soetomo Surabaya in 2019 with secondary data from medical records. The results of this study provide data on the number of cases, gender, age, CD4 levels and types of mucocutaneous manifestations in HIV AIDS patients that can be used as a basis and reference in further studies related to CD4 levels in HIV AIDS patients who have mucocutaneous manifestations. However, knowing the relationship between CD4 levels and mucocutaneous manifestations in HIV patients can be a clinical guide in determining the diagnosis and prognosis of advanced stages of HIV so that adequate therapy can be given and may help to reduce morbidity and mortality in HIV patients.

METHODS

This study was an analytical study with a retrospective cross-sectional design. The subjects were patients with a diagnosis of HIV-AIDS who had mucocutaneous manifestations. Mucocutaneous manifestations are clinical manifestations of skin and mucosa. There are 3 types of mucocutaneous manifestation that was evaluated in this study; the first was dermatoses infections, which can be caused by bacteria such as pyoderma and syphilis, caused by a virus such as herpes, varicella-zoster, molluscum contagiosum and human papillomavirus, caused by fungal such as candidiasis, dermatophytosis and systemic fungal infection. The second was non-infection dermatoses such as psoriasis vulgaris, drug eruption, xerosis, eosinophilic folliculitis, popular pruritic eruption and seborrheic dermatitis. The third was cutaneous malignancies, such as Kaposi sarcoma, squamous cell carcinoma, basal cell carcinoma and melanoma.

The data of the present study was obtained from a number of 614 HIV-AIDS patients with mucocutaneous manifestations who were treated at UPIPI RSUD Dr. Soetomo Surabaya in 2019, but only 149 patients met the inclusion criteria. Total sampling was used in this study. The inclusion criteria in this study were all patients diagnosed with HIV-AIDS (using Rapid Test of HIV) with mucocutaneous manifestations (new and controlled patient, with or without HAART), which were treated in the inpatient and outpatient

installations of the Intermediate Care and Infectious Diseases of Dr. Soetomo General Academic Hospital Surabaya in 2019, which had CD4 count data. The exclusion criteria were missing medical records. The CD4 count is an assessment test that measures the ratio of CD4 cells in the human body. The purpose of the CD4 count was to determine the health of immune system levels in patients affected with HIV (Human immunodeficiency virus) infection. The diagnosis was established by symptom-direct examination and laboratory findings. The data was only taken once, and there were no follow conducted.

The statistical relationship was identified and analyzed using the SPSS version 17 program. The data were categorized and arranged in an SPSS sheet for result analysis and tabulation. The test used Chi-Square and Spearman, and it was declared significant if < 0.05 . The research was conducted on the inpatient and outpatients of the Intermediate and Infectious Diseases Treatment Unit (UPIPI) RSUD Dr. Soetomo Surabaya, Indonesia. The duration of the study was

carried out starting from April 2020 to April 2021. The present research was approved and reviewed by the Ethical Committee (Reference no. 0032/LOE/301.4.2/VI/202) of Dr. Soetomo General Teaching Hospital situated in Surabaya, Indonesia.

RESULTS

The results of this study provide data on the number of cases, gender, age, CD4 levels and types of mucocutaneous manifestations in HIV AIDS patients that can be used as a basis and reference in further studies related to CD4 levels in HIV AIDS patients who have mucocutaneous manifestations. Out of the 149 patients who participated in the study, the highest CD4 cell count was 1,161 cells/mm³, and the lowest was 1 cell/mm³. Table 1 shows the baseline characteristic of this study. Distribution of CD4+ levels, there were CD4+ less than 200 in 96 patients (64.4%), CD4+ 200-500 in 42 patients (28.1%), CD4+ more than 500 in 11 patients (7.3%). The distribution of sex in this study is reported in Table 2. The majority of the cases were male, 111 patients (74.5%),

Table 1. Baseline Characteristics of subjects.

Characteristic	Frequency & Percentage (%)
CD4 (cell/mm³)	
< 200	96 (64.4)
200-500	42 (28.2)
> 500	11 (7.4)
Total	149 (100)
Gender	
Man	111 (74.5)
Woman	38 (25.5)
Total	149 (100)
Age (years)	
< 4	2 (1.3)
5 - 14	2 (1.3)
15 - 19	2 (1.3)
20 - 24	14 (9.4)
25 - 49	105 (70.5)
> 50	24 (16.2)
Total	149 (100)
Risk Factor	
Heterosexual	72 (48.3)
Homosexual	31 (20.8)
Bisexual	1 (0.7)
Injecting Drug User (IDU)	1 (0.7)
Maternal	3 (2.0)
No data	41 (27.5)
Total	149 (100)

while the female was 38 patients (25.5%). The male and female ratio is about 2.92:1. The majority of the cases were male, 111 patients (74.5%), while the female was 38 patients (25.5%). The male and female ratio is about 2.92:1. According to the age

division determined by the Indonesian Ministry of Health, the average age of the patients was 36 ± 10.87 years. The youngest patient was one year old, and the oldest was 65 years old. Most cases of HIV with mucocutaneous manifestations were found in the age group of 25-49 years, as many as 105 patients (70.5%). Based on the distribution of risk factors for HIV and AIDS patients with mucocutaneous manifestations, most of them were heterosexual, as many as 72 patients (48.3%), homosexual 31 patients (20.8%), bisexual one patient (0.7%), parenteral three patients (2.0%) and injecting drug user one patient (0.7%).

It was found that 149 patients had one or more skin manifestations. There are three groups of mucocutaneous manifestations: infectious, non-infectious, and malignancy, and there are 12 types of mucocutaneous manifestations. The most common infection found in this study was a fungal infection, with 30.2%, followed by non-infectious cases were PPE (23.3%). In this study, only two cases of malignancy were found in the form of lymphoma, but because they did not have data on CD4 levels and were not included in the inclusion criteria (Table 2).

In the CD4 category < 200 and 200-500, mostly found in the infectious group (72.5% and 23.3%), while for the CD4 category > 500 , in the non-infectious manifestation group (9.5%). Distribution for the type of disease from

Table 2. Distribution of mucocutaneous manifestations.

Category of Mucocutan manifestation	Diseases	Total n (%)
Infections		120 (55.8)
Bacterial	Pyoderma	10 (4.7)
	- Furuncles: 1	
	- Carbuncle: 1	
	- Secondary infection: 8	
Syphilis	Syphilis	12 (5.5)
	- Secondary: 6	
	- Latency: 6	
Fungal	Mucocutaneous candidiasis	65 (30.2)
	- Cutaneous candidiasis: 1	
	- Oral Candidiasis: 64	
	Dermatophytosis	8 (3.7)
	- Tinea corporis: 3	
	- Tinea pedis: 2	
- Tinea barbae: 1		
- Tinea cruris: 2		
Virus	Human papillomavirus infection	15 (6.9)
	- Condyloma Acuminata: 14	
	- Verruca: 1	
	Herpes simplex virus infection	1 (0.5)
	- Herpes Genital: 1	
Herpes Zoster	8 (3.7)	
Molluscum contagiosum	1 (0.5)	
Non-infections		95 (44.2)
	Seborrheic Dermatitis	15 (6.9)
	Pruritic Papular Eruption (PPE)	50 (23.3)
	Xerosis	15 (6.9)
	Drug reactions	15 (6.9)
	- Steven Johnson Syndrome: 2	
	- Morbiliform exanthem: 1	
	- Other drug eruptions (no specific data): 12	

Table 3. Distribution of CD4+ counts in each type of mucocutaneous manifestation of HIV and AIDS patients with mucocutaneous manifestations at Dr. Soetomo General Teaching Hospital Surabaya during 2019.

No.	Type of mucocutaneous manifestation	CD4 levels (cells/mm ³)			Total
		< 200 (%)	200-500 (%)	>500 (%)	
1	Pyoderma	4 (2.7)	4 (7.8)	2 (14.3)	10 (4.7)
2	Syphilis	3 (2.0)	7 (13.7)	2 (14.3)	12 (5.5)
3	Human papillomavirus infection	10 (6.7)	4 (7.8)	1 (7.1)	15 (6.9)
4	Herpes simplex virus infection	1 (0.7)	0 (0)	0 (0)	1 (0.5)
5	Herpes Zoster	7 (4.6)	1 (2.0)	0 (0)	8 (3.7)
6	Molluscum contagiosum	1 (0.7)	0 (0)	0 (0)	1 (0.5)
7	Mucocutaneous candidiasis	54 (36.0)	11 (21.6)	0 (0)	65 (30.2)
8	Dermatophytosis	7 (4.6)	1 (2.0)	0 (0)	8 (3.7)
9	Seborrheic Dermatitis	8 (5.3)	3 (5.9)	4 (28.6)	15 (6.9)
10	Pruritic Papular Eruption (PPE)	36 (24.0)	12 (23.5)	2 (14.3)	50 (23.3)
11	Xerosis	9 (6.0)	4 (7.8)	2 (14.3)	15 (6.9)
12	Drug reaction	10 (6.7)	4 (7.8)	1 (7.1)	15 (6.9)

the opportunistic infection group in the CD4 group, CD4 levels < 200, was found to be the most in the manifestations of mucocutaneous candidiasis and PPE, are 36.0% and 24.0%, respectively. CD4 levels of 200-500 were also the most common in the manifestations of mucocutaneous candidiasis and PPE, obtained at 21.6% and 23.5%, respectively. The CD4 level group > 500 was found the most in manifestations of seborrheic dermatitis (28.6%) (Table 3).

Analysis of the relationship was carried out between the infectious and non-infectious mucocutaneous manifestations on CD4 levels using the chi-square statistical test. The result obtained a p-value of 0.447, which indicates the value is > 0.05, meaning there is no significant/significant relationship between CD4 and mucocutaneous manifestations in the infectious and non-infectious groups (Table 4).

One hundred forty-nine data can be analyzed related to the relationship between CD4 levels and the type of mucocutaneous manifestations; of the 149 data obtained, 215 types of disease manifestations can be analyzed for the relationship. There was a significant relationship between CD4 levels in patients with syphilis infection ($P = 0.002$; Contingency coefficient 0.231), mucocutaneous candidiasis ($P = 0.006$; Contingency coefficient 0.213), and seborrheic dermatitis ($P = 0.005$; Contingency coefficient 0.218). Analysis of the ratio of the risk of mucocutaneous manifestations to CD4 levels showed that pyoderma and syphilis infections were significantly related to the condition of CD4 cell count of 200 cells/mm³ with a risk of 3.7 times and 7.8 times compared to CD4 < 200 cells/mm³. On the other hand, candidiasis infection was higher in conditions of CD4 count < 200 cells/mm³ with a significant difference and 0.3 times risk than CD4 200 cells/mm³.

DISCUSSION

Several studies have been conducted regarding skin disorders in HIV-positive patients, but the relationship between mucocutaneous lesions and CD4 cell counts has rarely been studied.⁸ The main target of HIV is the CD4 cell population. The progressive decline in the number

and function of the CD4 cell population is one of the most striking and consistent immunological features of HIV-associated disorders. In general, CD4 cell counts decreased as HIV disease progressed.^{9,10} Atypical features and severity of skin disease are what generally lead to the diagnosis of HIV infection.⁵ In a country like Indonesia, it is essential to identify skin markers that will predict the degree of immune suppression, as CD4 counts may not be possible in all patients regularly.

In this study, men made up 74.5%, while women made up 25.5% of patients. They were dominated by a male compared to females, with a male: female ratio of 2.92:1. The majority of patients in this study were 25-49 years age group, as many as 105 patients (70.5%). It is in line with data from the Directorate General of P2P sourced from the HIV, AIDS, and STI Information System (SIHA) in 2019. The fourth quarter stated that cases of HIV and AIDS in men were higher than in women. This is probably due to the increasing number of men who have sex with men (MSM) by practicing unsafe sex and the use of intravenous drugs (IVDU), which men dominate.⁷

HIV is spread through sexual contact with an infected person, contact or transfusion with infected blood, from mother to child, and sharing contaminated needles. In this study, the most frequent transmission mode was heterosexual (48.3%), followed by a homosexual (20.8%). This result may be due to patient reluctance to disclose precise information due to social and cultural differences in our region. Kamat et al. also reported heterosexuality as the most common mode of transmission, as much as 67.7%.¹¹ In fact, the heterosexual route continues to be the most common route of transmission reported worldwide.¹²

A decrease in the CD4 count is a sign of disease progression in HIV/AIDS. Mucocutaneous manifestations may increase with HIV progression and a decrease in CD4 cell count.¹³ It is thought that the incidence and severity of skin disorders increase with decreased immune function.⁹ In this study, 149 patients (24.3%) were examined for CD4+, obtained CD4+ less than 200 as many as 96 patients (64.4%), CD4+ 200-

500 as many as 42 patients (28.1%), CD4+ more than 500 as many as 11 patients (7.3%). Following the study of Britto et al., it has a higher incidence of skin manifestations in the advanced and severe immunosuppression categories.⁵

Mucocutaneous manifestations of HIV can be found in cases of infection, not infection, and tumors.¹⁴⁻²² In developed countries, non-infectious are more common in HIV patients.¹³ Mucocutaneous manifestations in HIV/AIDS patients in Indonesia may be different from those in other countries because of differences in skin pigmentation, climate, hygiene, genetics, environment, demographics, and behavioral patterns cause clinical manifestations and epidemiological patterns, which differ from developing countries such as Indonesia. In this study, the group with the most mucocutaneous manifestations was infection as many as 120 cases (55.8%); the second most was the inflammatory or non-infectious group, with 95 cases (44.2%). In this study, 2 cases of malignancy were found in the form of lymphoma, but because they did not have data on CD4 levels, they were not included in the study inclusion criteria.

In this study, from 3 groups of mucocutaneous manifestations that had CD4 data, there were 12 types of mucocutaneous manifestations: pyoderma infection, syphilis, human papillomavirus infection, herpes simplex (herpes labialis or genital herpes), herpes zoster, molluscum contagiosum, candidiasis, dermatophytosis, dermatosis seborrheic, PPE, xerosis, and drug eruptions. From the infection group, it was found that most cases were fungal infections which were dominated by mucocutaneous candidiasis (30.2%). These results agree with the study reported by Mirnezami et al. and Pudjiati et al.^{8,13} It can be due to Indonesia's tropical climate with relatively high humidity levels, making various germs, including fungal infections, easy to breed.¹³ The most non-infectious cases in this study were PPE in 50 patients (23.3%). This figure is more significant than the research results by Abhinandan and colleagues, who also showed that PPE was the most common non-infectious manifestation (13%).¹⁹

HIV infection impairs the immune system, leaving people infected with

Table 4. Analysis of CD4 Relationship Test with Types of Mucocutaneous Manifestations of HIV and AIDS patients with mucocutaneous manifestations at Dr. Soetomo General Academic Hospital Surabaya during 2019.

Mucocutan manifestations	N (%)	CD4 levels (n)			r***	p-value
		< 200	200-500	> 500		
Pyoderma	10 (4.6%)	4	4	2	0.157	0.066
Syphilis	12 (5.6%)	3	7	2	0.231	0.002**
Human papillomavirus infection	15 (6.9%)	10	4	1	0.020	0.960
Herpes simplex virus infection	1 (0.5%)	1	0	0	0.045	0.804
Herpes Zoster	8 (3.7%)	7	1	0	0.079	0.507
Molluscum contagiosum	1 (0.5%)	1	0	0	0.045	0.804
Mucocutaneous candidiasis	65 (30.2%)	54	11	0	0.213	0.006*
Dermatophytosis	8 (3.7%)	7	1	0	0.079	0.507
Seborrheic Dermatitis	15 (7.0%)	8	3	4	0.218	0.005**
Pruritic Papular Eruption (PPE)	50 (23.3%)	36	12	2	0.056	0.712
Xerosis	15 (7.0%)	9	4	2	0.081	0.489
Drug reaction	15 (7.0%)	10	4	1	0.020	0.960

*Test used Chi-Square is declared significant if <0.05 . ** test used Spearman is declared significant if <0.05 . *** r = strength of the relationship

HIV susceptible to various infections. Opportunistic infectious conditions in HIV patients are a significant cause of mortality and morbidity. The effect of HIV on the immune system is monitored by measuring the number of CD4 lymphocytes in the blood.^{13,22} In this study, the distribution of CD4 < 200 and 200-500 categories were more common in the infectious group (72.5% and 23.3%), while for the > 500 CD4 categories, more occurred in the non-infectious manifestation group (64.3%). HIV patients with high CD4 cell counts have an excellent immune response to respond the specific pathogens.^{9,13,22}

CD4 levels < 200 were found the most in mucocutaneous candidiasis and PPE, 36.0% and 24.0%, respectively. CD4 levels of 200-500 were also found the most in the manifestations of candidiasis and PPE, namely 21.6% and 23.5%, respectively. The CD4 level group > 500 was found the most in manifestations of seborrheic dermatitis (28.6%). Fungal infections are most common at low CD4 cell counts. HIV infection can change the course of the fungal disease so that the lower the CD4 count causes, the higher the fungal infection.¹³ PPE constitutes the majority of cases in inflammatory or non-infectious dermatoses.¹² In A study conducted in Thailand, Wichai et al. found PPE as the most common skin finding. Another study in Iran reported an incidence of

36.7%.²⁰ PPE may appear as an early skin disease with a high CD4 cell count and is described as a stage II disease by WHO.¹² Several studies have reported widespread atypical seborrheic dermatitis in patients ranging from 15.62% to 83%. The cause of seborrheic dermatitis is unknown, but many researchers believe that changes in the immune system in HIV-AIDS, altering the skin's response to the fungus *Pityrosporum ovale*, lead to higher infection rates.²⁰

HIV-AIDS patients experience immunologic dysfunction, and with the diversification of therapeutic drugs, the incidence of drug eruptions among these patients is usually higher than that of the general population.²¹ In our study, drug eruption was found in 6.9% of patients, with the most having a CD4 count < 200, this result is lower than reported in the literature.²¹ Drug reactions include maculopapular, urticarial rash, and Stevens-Johnson syndrome. The principal causative agent noted was Nevirapine. The lower incidence in our study can be explained by the fact that ARV itself improves the general condition of the patients. The current principle of ARV is to use three types of drugs, all three of which must be absorbed and in therapeutic doses in the blood, known as highly active antiretroviral therapy (HAART) and often shortened to antiretroviral therapy (ART). It has been shown that patients with

CD4+ cell count < 200 are more likely to have a drug eruption, which is associated with immune function status. Therefore, patients should evaluate the risk when using different hypersensitivity drugs.²¹

The results showed the analysis of the relationship between the group of infectious and non-infectious mucocutaneous manifestations with CD4 levels based on the Chi-Square Test and obtained a p-value of 0.447. The p-value is > 0.05, which means there is no significant relationship between CD4 and the group of infectious and non-infectious mucocutaneous manifestations; this is the same as reported in a study in Pakistan. Wichai et al. even reported an inverse relationship between CD4 cell count and skin disease incidence and severity. Therefore, this correlation is still controversial.⁴

We carried out the further analysis in this study by looking for the relationship between CD4 levels and each of the 12 types of mucocutaneous manifestations in this study, such as pyoderma infection, syphilis, human papillomavirus infection, herpes simplex, herpes zoster, molluscum contagiosum, candidiasis, dermatophytosis, seborrheic dermatitis, PPE, xerosis, and drug eruptions. Found a significant relationship between CD4 cell count and mucocutaneous candidiasis (P = 0.003) and has a weak relationship strength of 21% (r = 0.213). It is in line with

a similar study conducted by Abihandan et al. and Mirnezami et al. A CD4 cell count of fewer than 200 cells/mm³ was significantly associated with a higher number of mucocutaneous disorders and the development of candidiasis.¹⁹ Another study also found candidiasis as a mucocutaneous disorder with a significant association with low CD4 cell count, which is also in line with previous studies.⁸

The odds ratio was calculated to determine the level of risk of mucocutaneous disease in HIV/AIDS patients by changing the CD4 group into two categories, namely < 200 and 200 cells/mm³. Pyoderma infection was significantly associated with a CD4 cell count of 200 cells/mm³ with a risk of 3.7 times compared to CD4 < 200 cell/mm³. Likewise, syphilis has a significant relationship with a CD4 cell count of 200 cells/mm³ with a risk of 7.8 times compared to CD4 < 200 cells/mm³. On the other hand, mucocutaneous candidiasis infection was higher in conditions of CD4 count < 200 cells/mm³ with a significant difference and 0.3 times risk compared to CD4 200 cells/mm³. These results are different from similar studies conducted by other researchers. Pudjiati et al. reported that a lower CD4 cell count (< 200 cells/mm³) increased the risk of fungal infection by 3.8-fold. A higher CD4 cell count (> 200 cells/mm³) increases the risk of viral infection by about 2.5-fold and parasitic infection by 5-fold.¹³ Goh et al. found that the risk of developing PPE was three times higher in patients with CD4 counts below 200 cells/mm³. Sanchez et al. found that 80% of their patients had CD4 counts <100 cells/mm³. The higher mean CD4 cell count in the current study may be because 90% of patients with PPE are on ART and may be due to IRIS.¹⁹

Lowe and others reported that PPE and molluscum contagiosum was most commonly seen in patients with lower CD4 cell counts. According to Noruka's study, PPE was most commonly found at CD4 counts < 200, and seborrheic dermatitis was observed in patients with CD4 counts between 200 and 500. In Goh's study, CD4 cell count < 200 was strongly associated with psoriasis and drug reactions.⁸ However, a significant association between PPE and seborrheic

dermatitis on CD4 levels was not found in our study. The differences in the results of these different studies can be explained by variations in sample size, disease stage, route of infection, and regional patterns of reported disease.

HIV/AIDS patients are at high risk for malignancies, such as Kaposi's sarcoma, non-Hodgkin's lymphoma, and cervical carcinoma. These three malignancies are often called AIDS-defining conditions. If one of the three malignancies is found, it can indicate the course of HIV infection has reached the AIDS stage. The relationship between HIV infection and certain types of malignancy is still unexplained, possibly related to a decrease in the immune system.¹³ In this study, only two lymphoma cases were found; this could be due to other malignancies in patients who were not screened for HIV. In addition, no data were obtained regarding CD4 levels in patients, so an analysis of the relationship could not be carried out.

This study has some limitations because it was conducted in a tertiary care hospital, so the manifestation may be different from patients in hospitals in primary and secondary services. It is important to plan and carry out research using larger sample sizes in different areas, which will help in better interpretation of the population. The small number of patients who have CD4 levels checked is also a limitation in this study, so the monitoring of immune status through CD4 level examinations needs to be further improved so that it can provide guidelines for possible interventions and better prognostics.

CONCLUSION

Manifestations of mucocutaneous disorders occur throughout the course of HIV infection. Several mucocutaneous manifestations can be considered as predictors of advanced HIV infection (low CD4 level), which were infections, syphilis, and in this study. According to the distribution of CD4 results with mucocutaneous manifestations, it was found that CD4 < 200 cells/mm³ and 200-500 cells/mm³ in HIV/AIDS patients mostly related to infections categorized diseases, especially as mucocutaneous candidiasis. Moreover, CD4 > 500 cells/mm³ were also found in non-

infectious categorized diseases, with the most manifestations being seborrheic dermatoses. This study has some limitations because it was conducted in a tertiary care hospital, and there was no follow-up to observe the development or deterioration of dermatoses. It is important to plan and carry out research using larger sample sizes in different areas, which will help in better interpretation of the population.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ETHICAL CLEARANCE

The present research was approved and reviewed by the Ethical Committee (Reference no. 0032/LOE/301.4.2/VI/202) of Dr. Soetomo General Teaching Hospital situated in Surabaya, Indonesia.

AUTHOR CONTRIBUTION

All authors contributed to the study, including conceptual framework, design, data collection, and data analysis to report study results for publication.

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