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Bali Medical Journal

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PUBLICATION TYPE	ISSN	COVERAGE	INFORMATION
Journals	20891180, 23022914	2020-2021	Homepage How to publish in this journal srimaliawan@unud.ac.id

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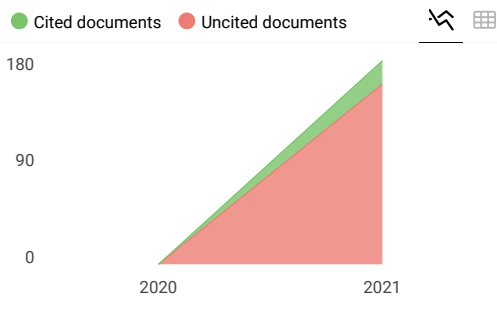
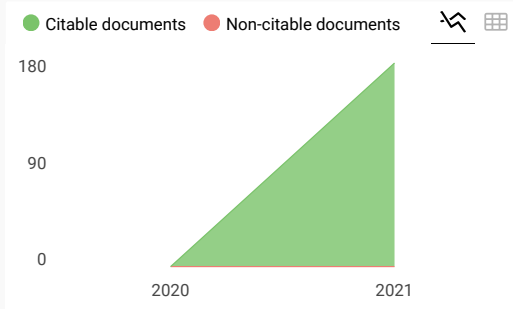
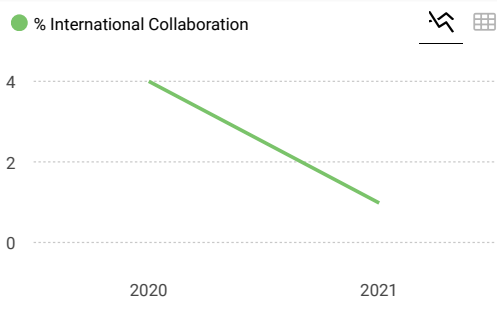
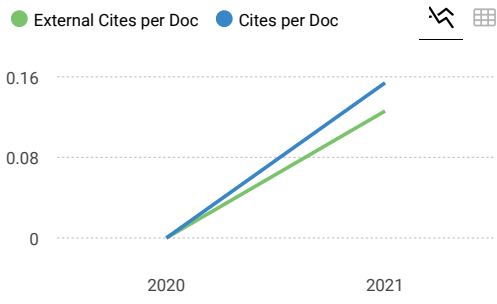
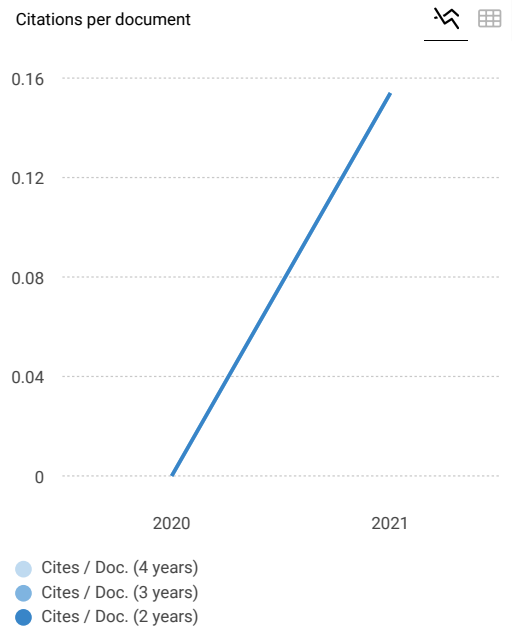
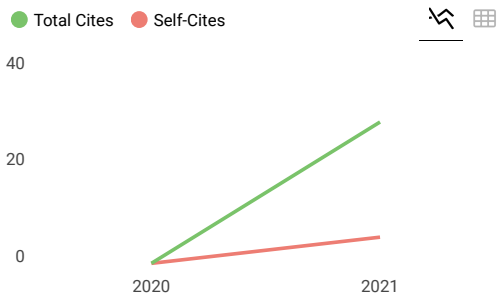
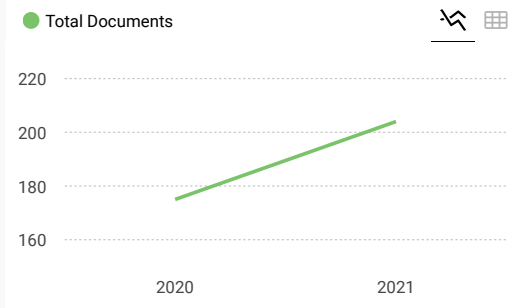
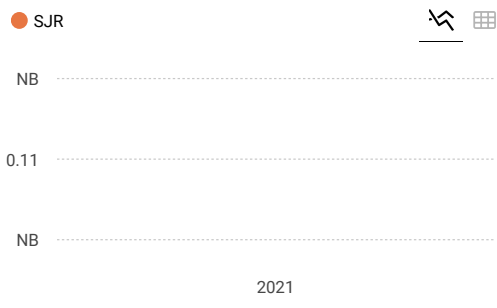
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Dennis Chrissandy Wasito, Iskandar Ali, Fransiska Kusumowidagdo, I Gusti Bagus Adria Hariastawa

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Tracing management and epidemiological characteristics of close contact COVID-19 in primary health care
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Dwi Yulianingsih Putri Hanardi, Erna Rochmawati

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Diagnostic test of Immature Granulocyte Ratio (IG Ratio) to detect Early-Onset Neonatal Sepsis (EONS)
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3795>)

Sherly Karolina Simanjuntak, Sianny Herawati, Made Sukmawati, I Wayan Putu Sutirta Yasa, Ni Kadek Mulyantari, Anak Agung Wiradewi Lestari, I Nyoman Wande, I Made Ady Wirawan

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Factors influencing Bromage score in post-spinal anesthesia patients (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3435>)

Resiana Karnina, Nandya Satyaning Rahayu, Muhammad Faruk

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Clinical characteristics and mortality associated with COVID-19 in islamic hospital of Jemursari, Surabaya, Indonesia: A hospital-based retrospective cohort study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3541>)

Evi Awwaliyah, Hotimah, Michio Shimabukuro

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Effect of tartrazine on blood urea nitrogen, creatinine levels, and renal tubular necrosis in adult male Wistar rats (*Rattus norvegicus*): an experimental study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3623>)

Mulyati Sri Rahayu, Sri Wahyuni, Idha Fitriani, Habib Budiman Agung

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Transformation of the learning system in nursing education after the COVID-19 pandemic (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3720>)

Sulastri, Wachidah Yuniartika, Diah Ayu Agus Triana, Giyoto

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Evaluation of dermoscopic photoaging score among multiethnic in Medan, Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3810>)

Nelva Karmila Jusuf, Imam Budi Putra, Medina Muslim

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A comparative study of full-thickness wound healing in rats using Nile tilapia skin and fresh human amnion
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3927>)

Nyssa Claresta Adhya Sastri, Iswinarno Doso Saputro, Lobredia Zarasade

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Association between metabolic syndrome and knee osteoarthritis (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3454>)

Ardyarini Dyah Savitri, Lysa Veterini, Meidyta Sinantryana Widayawari , Diaz Syafrie Abdillah

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Distribution of blood-added tablets in adolescent girls in the COVID-19 pandemic (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3546>)

Pratiwi Hariyani Putri , Dini Setiarsih, Rizki Amalia

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Liver function characteristics of COVID-19 patients with obesity at Dr. Soetomo Hospital: case series
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3727>)

Erwin Maulana Farmanda Putra, Ummi Maimunah

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Clinicopathological characteristics and possible risk factors for extrauterine metastases in endometrial carcinoma
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3820>)

Teuku Mirza Iskandar, Very Great Eka Putra, Ediwibowo Ambari, Endy Cahyono, Lubena

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The effect of pursed-lips breathing and diaphragm exercises on the quality of life of COPD patient assessed by six-minutes walk test (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3474>)

Mulyadi, Ida Muna Junita, Teuku Zulfikar, Nurrahmah Yusuf, Mulkan Azhary, Hotimah Masdan Salim

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Acceptance of interprofessional education (IPE) for educators at health-based faculty universitas nahdlatul ulama Surabaya (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3495>)

Wiwik Afridah, Trimartiana , Prihartini Widiyanti, Mochammad Bagus Qomaruddin

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Frequency of Interleukin-6 rs 1800796 (-572G/C) and 2069837 (intron 2A/G), TNF- α rs1800750 (-376G/A), and 1800629 (-308G/A) polymorphism in COVID-19 patients with clinical degrees in Central Java (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3552>)

Reviono, Hendrastutik, Yulia Sari, Betty Suryawati, Darmawan ismail, Ketut Putu Yasa

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Fatigue and excessive daytime sleepiness among nurses (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3746>)

Septian Mixrova Sebayang, Made Suandika, Ita Apriliyani, Suci Khasanah, Asmat Burhan, Noor Yunida Triana, Dwi Astuti

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The pattern of osteocyte in dental socket bone regenerative induced by hydroxyapatite bovine tooth graft (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3844>)

Nanik Zubaidah, Sri Kunarti, Nadira Nurin Febrianti, Arif Rahman Nurdianto, Wanda Oktaria, Muhammad Luthfi

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Strengthening community roles to reduce stunting in COVID-19 pandemic in indonesia rural areas: capacity building program for cadres and local government (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3753>)

Supriyatningsih Wenang, Ima Rismawati, Lidia Febrianti, Bambang Edi Susyanto, Gina Puspita, Alfaina Wahyuni, Arlina Dewi, Dianita Sugijo, Sutantri, Diyah Nahdiyati, Anang Widhi Nirwansyah

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A study of molecular docking of l-tryptophan ligand as a compound in pineapples and bananas binding with the human serotonin transporter (SERT) (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3526>)

Susy Purnawati, Luh Putu Wrasiasi, Cokorda Bagus Jaya Lesmana, Sandra Megantara, Ronny Lesmana

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Fibrin glue as a novel therapy for contracted socket in comparison to mitomycin-c and triamcinolone acetonide at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3687>)

Firda Ayu Muthie, Evelyn Komaratih, Sutjipto, Dyah Fauziah, Budi Utomo

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The impact of age, gender, family history of allergy, clinical symptoms, and duration of illness on flare diameter of skin prick test (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3870>)

Uuk Rihuh Kusuma Wardana, Anang Endaryanto, Cita Rosita Sigit Prakoeswa

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Phytochemical screening, antioxidant activity and cytotoxicity assay from noni juice and fermented noni (*Morinda citrifolia* L.) (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3534>)

Handayani, Devyana Dyah Wulandari, Devyani Diah Wulansari

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Calming effect of Javanese Handwriting Calligraphy, preliminary study based on neuroaesthetics
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Arman Yurisdaldi Saleh, Miky Miky Endro Santoso, Wawan Murwantara, Retno Yulianti, Imam Prabowo

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Factors related to family resilience during the COVID-19 pandemic (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3703>)

Martina Pakpahan, Lia Kartika, Mega Sampepadang

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Intensifying self-awareness of undergraduate students toward hypertension risk factors through health education
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3784>)

Ambar Relawati, Dewi Maulidawati

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Effects of probiotics and high fructose diet on De Ritis ratio, TGF-B levels, and liver histopathology of Sprague Dawley rats
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3397>)

Ninung Rose Diana Kusumawati, Damianus Galih Panunggal, Maria Mexitelia, Magdalena Sidhartani, Agustini Utari

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Parenting stress against symptoms of gadget addiction in elementary school age during the COVID-19 pandemic
(<https://www.balimedicaljournal.org/index.php/bmj/article/view/3539>)

Nur Hidayah, Esti Yunitasari, Hanik Endang Nihayati, Imamatul Faizah, Ratna Yunita Sari

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Restarting living donor kidney transplant during COVID-19: a single center experience (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3615>)

Mochammad Fairuz Zahran, Tanaya Ghinorawa

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Expression of Na⁺/K⁺ATPase and changes of corneal endothelium cell density after phacoemulsification with hypothermic perfusion (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3718>)

Ratih Justitia Kartika, Reni Prastyani, Dyah Fauziah, Soenarnatalina Melaniani, Wimbo Sasono

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The Effect of Beta vulgaris L. on the Malondialdehyde Levels in Male Wistar Rats Exposed to Cigarette Smoke (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3806>)

Alya Berliana Suharso, Puspita Kusuma Dewi, Edward Kurnia Setiawan Limijadi, Amallia Nuggetsiana Setyawati

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Relationship between Vitamin D Levels and Platelet Function in the Elderly Patients with Coronary Heart Disease (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3911>)

Charles Limantoro, Catharina Suharti, Trilaksana Nugroho, Friska Wilda Wijaya

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Knowledge and parity prevention of anemia in pregnancy (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3451>)

Tutik Ekasari, Mega Silvian Natalia, Muthmainnah Zakiyyah

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Parental support is important to improve clean and healthy living behavior for school-age children during the COVID-19 pandemic (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3544>)

R. Khairiyatul Afyah, Ratna Yunita Sari, Rusdianingseh, Yurike Septianingrum, Ika Mardiyanti, Robi Is Maulana, Firman Suryadi Rahman

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Stromal Tumor Infiltrating Lymphocytes (TIL) as a potential prognostic biomarker for recurrence in Locally Advanced Breast Cancer (LABC) patients (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3724>)

Dannu Novriandhika, Dwi Hari Susilo, Dyah Fauziah, Priangga Adi Wiratama, Desak Gede Agung Suprabawati

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Application of DNA Barcoding for authentication of Balinese traditional medicinal plant Purnajiwa (*Kopsia arborea* Blume. and *Euchresta horsfieldii*) (Lesch.) Benn (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3815>)

Putu Eka Pasmidi Ariati, Maria Malida Vernandes Sasadara, I Gede Putu Wirawan, Made Sritamin, I Ketut Suada, I Nyoman Wijaya, Rindang Dwiyani, I Putu Sudiarta, Ida Ayu Putri Darmawati

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A pilot study of new scoring system severity of striae distensae (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3968>)

Imam Budi Putra, Nelva Karmila Jusuf, Alviera Yulindra Amal

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The effect of oral phenytoin and vitamin C therapy on enterocutaneous fistula healing (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3469>)

Yohannes Sugiarto, Ignatius Riwanto, Trilaksana Nugroho

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Acceptance of the covid-19 vaccine based on health belief model (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3549>)

Eppy Setiyowati, Rahayu Anggraeni, Priyo Mukti Winoto, Domingas da Silva Soares Pereira, Paulo Lopes, Aquino Tinos Martins

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The effect of Curcuma longa on fasting blood glucose, MMP-9 and IFN- γ in diabetes mellitus: an experimental study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3648>)

Shafira Zahra Ovaditya, Surya Pratama Brilliantika, Chodidjah Chodidjah, Titeik Sumarawati

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Expression of Superoxide Dismutase-1 (SOD-1) and changes of corneal endothelial morphology after phacoemulsification with hypothermic perfusion (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3734>)

Afia Nuzila Fadhlina, Luki Indriaswati, Nurwasis, Dyah Fauziah, Mahmudah

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Association between the levels of muscle-specific creatinine kinase (CK-MM) and the incidence of persistent myalgia in COVID-19 survivors (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3827>)

Aria Adhiatma, Christrijogo Sumartono Waloejo, Bambang Pujo Semedi, Hamzah , Prihatma Kriswidyatomo, Pudji Lestari

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Relationship between self-regulation with self- acceptance of hypertension patients during the covid- 19 pandemic period in Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3499>)

Umdatul Soleha, Ah Yusuf, Oedojo Soedirham, Ratna Yunita Sari, R. Khairiyatul Afiyah, Chilyatiz Zahroh, Immatul Faizah

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The correlation between the usage of kami pekarasa card (cards of pregnant mother for posyandu's members and villages authority holders) and the visit coverage of k4 pregnant mother during COVID-19 pandemic event (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3555>)

Iis Hanifah, Tutik Hidayati, Riska Faraswati

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Ultrasound assessment of femoral cartilage thickness among healthy Indonesian adults (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3667>)

Rita Vivera Pane, Aisyah, Hajar Ariani, Erwien Isparnadi, Aufar Zimamuz Zaman Al Hajiri, Albert Setiawan

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Histopathology of colorectal cancer in Cut Meutia Hospital, Aceh-Indonesia from 2017-2020 (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3750>)

Muhammad Sayuti, Muhammad Syahriza, Ghisca Chairiyah Ami

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The performance of various laboratory parameters to differentiate follicular thyroid carcinoma and follicular thyroid adenoma (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3521>)

Satriya Kelana, Dwi Hari Susilo, Sahudi

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Comparative effect of incentive spirometry and diaphragm breathing to functional capacity in COVID-19 patient in an isolated ward (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3579>)

Amien Suharti, Evi Rachmawati Nur Hidayati, Hafizia Asri Yusviani

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The sensitivity pattern of ciprofloxacin and amoxicillin in chronic suppurative otitis media (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3756>)

Lilis Suryani, Asti Widuri, Muhammad Kurniawan, Bombong Nurpagino

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Role of neutrophil gelatinase-associated lipocalin (NGAL) as a acute prerenal kidney injury marker: Exploring factors associated with its postoperative levels in hypotension-controlled otorhinolaryngology surgery (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3868>)

Andy Nauman Saputra, Prananda Surya Airlangga, Bobby Abdul Rahman, Edward Kusuma, Prihatma Kriswidyatomo, Christrijogo Sumartomo

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Risk Factors of Titanium Mesh Exposure: Experience from a Tertiary Referral Center (<https://www.balimedicaljournal.org/index.php/bmj/article/view/2428>)

Christian Beta Kurniawan, Akhmad Imron, Muhammad Rainda Farhan

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The relationship of parent's nutrition knowledge level and teacher's food parenting on nutritional status of pre-school aged children (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3532>)

Yanesti Nuravianda Lestari, Eko Farida, Nur Amin, Amelia Setyowati, Wiwik Afrida, Fifi Khoirul Fitriyah

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Serum ferritin level in pediatric patients with acute lymphoblastic leukemia (ALL) in the early stage of diagnosis and remission phase (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3595>)

Novia, Nelly Rosdiana, Supriatmo



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ORIGINAL ARTICLE

Correlation of chest radiography of confirmed COVID-19 patients with comorbid hypertension and diabetes mellitus (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3691>)

Ana Majdawati, Annisa

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Gut microbiome analysis in human living close to livestock at Mlati district, Sleman, Yogyakarta (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3774>)

Yulia Sari, Betty Suryawati, Ari Natalia Probandari, Hartono, Wayan Tunas Artama, Bambang Purwanto, Soetrisno

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ORIGINAL ARTICLE

Renal function features in pediatric acute lymphoblastic leukemia during high-dose methotrexate chemotherapy (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3890>)

Adkhiatul Muslihatin, Mia Ratwita Andarsini, Andi Cahyadi, Risky Vitria Prasetyo, I Dewa Gede Ugrasena, Maria Christina Shanty Larasanti

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The effect of discharge planning on the stability of blood sugar levels in type 2 diabetes mellitus patients (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3537>)

Difran Nobel Bistara, Erika Martining Wardani, Susanti, Andreas Putro Ragil Santoso, Abdul Hakim Zakkiy Fasya, Ary Andini

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ORIGINAL ARTICLE

Association between serum TNF- α level with the incidence of metastases in women with breast cancer in Dr. Soetomo General Hospital, Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3611>)

Rachman Efendi, Husnul Ghaib, Iskandar Ali



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ORIGINAL ARTICLE

Fibrin glue: an anti-fibrotic agent for contracted socket (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3707>)

Ivon Bremmy Wydha Saputro, Yulia Primitasari, Susy Fatmariyanti, Dyah Fauziah, Budi Utomo

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Carotid intima-media thickness in the first descendant of coronary artery disease patients with Apolipoprotein-E4 genotype (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3798>)

Ahmad Rafi Satrio Prayogo, Elvira Yunita, Rachmawaddah Yolanda, Ismir Fahri, Novriantika Lestari, Marisadonna Asteria, Ahmad Azmi Nasution, Jusup Endang, Sipriyadi, Ellen Maidia Djatmiko

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ORIGINAL ARTICLE

Clinical and laboratory comparison between End-Stage Kidney Disease patients with and without COVID-19: a cross-sectional study in a top referred hospital of West Nusa Tenggara (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3440>)

I Gede Yasa Asmara, I Gusti Ngurah Ommy Agustriadi, I Made Sujaya, Salim Said Thalib, Rina Lestari, Suryani Padua Fatrullah, Komang Sri Rahayu Widiarsari, Indana Eva Ajmala, Metta Octora

Online First: Sep 5, 2022 |

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A study of efficacy, safety, and acceptance of two combined oral contraceptive pills containing 150 mcg Levonorgestrel and 30 mcg Ethinyl Estradiol at Dr. Kariadi Hospital, Semarang, Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3629>)

Syarief Thaufik Hidayat, Hary Tjahjanto, Robert Eria, Yenny Kartika Gozali

Online First: Sep 27, 2022 |

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Soft skills elements in structured clinical skill assessment: a qualitative study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3721>)



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ORIGINAL ARTICLE

Bacterial colonization in atopic dermatitis (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3811>)

Deryne Anggia Paramita, Khairina, Nova Zairina Lubis

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ORIGINAL ARTICLE

The effects of oral antihistamines on the formation of granulation tissue on full-thickness wounds in white rats *Rattus norvegicus* (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3928>)

Taufiqur Rakhim Aditra, Agus Santoso Budi, Iswinarno Doso Saputro

Online First: Dec 20, 2022 |

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Antioxidant activity of *Tinospora crispa* extracted with different ethanol solvents (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3467>)

Renny Novi Puspitasari , Sri Agus Sudjarwo, Agung Pranoto , Achmad Basori

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Correlation of magnetic angiography with relative cerebral blood flow on arterial spin labeling using magnetic resonance imaging in acute ischemic stroke patients (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3547>)

Utami Ambarsari, Arif Faisal, Hari Basuki Notobroto, Erna Furaidah, Yunita Lestari Indrianto, Naura Anindya Candini

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Utilization of local culture "Bapalas Bidan" as a postpartum counseling media on contraception tools (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3641>)



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Ameliorative effect of 50% ethanol extract of moringa leaves (*Moringa oleifera* Lam.) on lead-induced oxidative stress in the liver of male wistar rat model (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3728>)

Agung Saprasetya Dwi Laksana, Lily Kusumasita , Falah Faniyah

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Transcortical selective amygdalohippocampectomy for intractable mesial temporal lobe epilepsy: a review of outcomes in a single center (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3475>)

Aris Catur Bintoro, Muhamad Thohar Arifin, Harsono, Amin Husni, Surya Pratama Brilliantika, Yuriz Bakhtiar, Novita Ikbar Khairunnisa, Rofat Askoro, Jacob Bunyamin, Soeharyo Hadisapurto, Zainal Muttaqin

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ORIGINAL ARTICLE

Exercise decrease the expression of MCP-1 in perivascular adipose tissue (PVAT) in obese mice (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3496>)

Hotimah Masdan Salim, Aisyah Aisyah, Michio Shimabukuro

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Stress, motivation, satisfaction, and learning achievement: A case study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3553>)

Widya Addiarto, Yulia Rachmawati Hasanah

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Visual science mapping and future direction of pediatric acupuncture: a bibliometric analysis from Scopus database and



VOSviewer (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3747>)

Selfi Handayani, Nanang Wiyono, M. Nur Dewi Kartikasari, Endang Listyaningsih Suparyanti, Annang Giri Moelyo, Balgis, Faizal Muhammad, Ahmad Fasichul Iman

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Circumcision in Bali? a survey of knowledge and attitude of Balinese parents toward their son's circumcision in elementary school Denpasar, Bali (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3516>)

I Wayan Jordan Junior, Rizky Darmawan, Dhanu Aryawangsa, Adi Satrya Palguna, Nindya Prahasari, Anak Agung Gde Oka

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Transcatheter aortic valve implantation: A review article (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3571>)

Starry Homenta Rampengan, Jansen Chitrahadinata

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The effect of intravenous remifentanyl and fentanyl postoperative delirium incidence in patients receiving elective orthopedic surgeries (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3851>)

Hanung Aryana, Dedi Susila, Belindo Wirabuana

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Granulocyte colony-stimulating factor therapy as a bridging treatment for pediatric decompensated liver cirrhosis prior to liver transplantation: an open-label randomized clinical trial (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3527>)

Tri Hening Rahayatri, Alida Harahap, Aryono Hendarto, Hanifah Oswari, Rianto Setiabudy, Akmal Taher

Online First: Sep 23, 2022 |

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ORIGINAL ARTICLE



Medico-socio-economic perspective of congenital hydrocephalus patients treatment in dr. Soetomo Academic General hospital, Surabaya, Indonesia (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3586>)

Heru Kustono, Muhammad Arifin Parenrengi, Arief Wibowo, Agus Turchan, Kurnia Kusumastuti, Asra Alfauzi

Online First: Dec 8, 2022 |

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ORIGINAL ARTICLE

Regenerative alveolar bone in dental sockets of diabetic wistar rats post tooth extraction (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3874>)

Nanik Zubaidah, Muhammad Luthfi, Wisnu Setyari, Retno Palupi, Nur Imamatul Ummah, Ardyta Lintang Maheswari, Arif Rahman Nurdianto, Fathillah Abdul Razak

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ORIGINAL ARTICLE

Anti-inflammatory effects and potential mechanisms of *Mitragyna speciosa* methanol extract on λ -karagenan-induced inflammation model (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3535>)

Hotimah Masdan Salim, Choirotussanijjah, Evi Sylvia Awwalia, Ilham Putera Alam

Online First: Sep 13, 2022 |

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ORIGINAL ARTICLE

Grape (*Vitis vinifera* L.) skin extract reduced levels of SGPT and SGOT and improved the liver tissue structure of Wistar rats (*Rattus norvegicus*) fed a high-cholesterol diet (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3602>)

Siti Maryam, Ni Kadek Alit Arsani, Sartika Tangguda

Online First: Oct 13, 2022 |

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ORIGINAL ARTICLE

Understanding the purchasing behaviors of halal cosmetics of teenagers in Indonesia using the theory of planned behavior and theory of consumption value (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3704>)

Titih Huriah, Iman Permana, Mega Octavia, Siti Hazariah Binti Abdul Hamid

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ORIGINAL ARTICLE

The Effect of chair-based exercise and vitamin d levels with hand grip strength in elderly woman (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3786>)

Dwi Ngestiningsih, M Agung Wibowo Wicaksono, Probosuseno, Yuswo Supatmo, Banundari Rachmawati

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ORIGINAL ARTICLE

Comparison of intestinal fatty acid binding protein (I-FABP) level between pre- and post-surgery and its associated determinants in patients with microscopic otorhinolaryngology surgeries (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3893>)

Yuda Atmajaya, Mohammad Satriyo Wibowo, Prananda Surya Airlangga, Maulydia, Prihatma Kriswidyatomo, Muhtarum Yusuf, Budi Utomo

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ORIGINAL ARTICLE

The effectiveness of the self-care management model in midwife care through android application as an effort to increase the ability of pregnant mothers in early detection of pregnancy at risk during the COVID-19 pandemic (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3430>)

Ika Mardiyanti , Annif Munjidah, Nanik Handayani, Siska Nurul Abidah, Hinda Novianti, Uliyatul Laili, Lailatul Khusnul Rizki

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ORIGINAL ARTICLE

Blockchain integration for hospital information system management (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3540>)

Naufal Adi Satrio, Sritrusta Sukaridhoto, M. Udin Harun Al Rasyid, Rizqi Putri Nourma Budiarti, Ilham Achmad Al-Hafidz, Evianita Dewi Fajrianti

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ORIGINAL ARTICLE

Implementation of the blood donation preservation strategy at Indonesian red cross (IRC) blood donor unit (BDU) Banda Aceh during the COVID-19 pandemic (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3622>)

Teuku Ilhami Surya Akbar, Maulana Ikhsa, Ratna Sari Dewi

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ORIGINAL ARTICLE

Systemic Lupus Erythematosus Flare Triggered by COVID-19 Infection: A Case-Based Review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3719>)

Maria Sarce Tio, Arundina Sanyoto

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Excessive physical exercise caused a decrease in CD4+ and Hematopoietic Stem Cell (HSC) levels in Wistar rats (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3809>)

Si Ngurah Oka Putrawan, I Made Jawi, I Wayan Putu Sutirta Yasa, Anak Agung Ngurah Subawa, Ida Bagus Putra Manuaba

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The effect of freeze-dried human amnion on New Zealand rabbit tendon healing (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3926>)

Melissa Anita Ayu Iustitiati, Sitti Rizalijana, Agus Santoso Budi

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Effect of aromatherapy blend essential oils (lemongrass and lemon) on sleep quality in pregnant women's third trimester (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3453>)

Fritria Dwi Anggraini , Siska Nurul Abidah, Esty Puji Rahayu, Fauziyatun Nisa

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The effect of syzygium polyanthum (wight) extract in histological changes of kidney in diabetic mice model (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3545>)

David Sajid Muhammad, Hotimah Masdan Salim, Cici Dita Virlliana, Adyan Donastin, Agus Aan Adriansyah

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ORIGINAL ARTICLE

Comparison of outcomes between a ruptured and unruptured intracranial aneurysm: results from an Indonesian cohort study (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3725>)

Julius July, Patrick Putra Lukito, Vanessa Angelica, Jeremiah Hilkiah Wijaya, Audrey Hamdoyo, Nyoman Aditya Sindunata, Rusli Muljadi

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ORIGINAL ARTICLE

The role of serum ferritin level and disease severity in COVID-19 with type 2 diabetes mellitus patients (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3818>)

Fauzia Noor Liani, Sony Wibisono Mudjanarko, Hermina Novida

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ORIGINAL ARTICLE

Formation of woven bone in orthodontic tooth movement tension areas after giving Mangostin by expression of Runx-2 and IL-10 (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3971>)

Ida Ayu Arnawati, I Ketut Sudiana

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ORIGINAL ARTICLE

The effect of Quran recitation on t-cell lymphocyte activity in mice model of breast cancer (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3473>)

Akbar Reza Muhammad, Yunyastiti D. Palupi, Mega Astri, Hafid Algristian

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ORIGINAL ARTICLE

Protective effect of lavender essential oils on depression and multi-organ stress (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3655>)

Hafid Algristian, Tri Wahyuni Bintarti, Rani Nur Mukaromatim Baroroh, Qorieatul Leila, Reina Ulfa, Amelia Krismawati, Mifa Nurdiana, Giftania Wardhani Sudjarwo, Adhi Wibowo Nurhidayat, Irawan Satriotomo, Retno Handajani

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Efficacy of therapeutic plasma exchange and convalescent plasma therapy in moderate-to-severe COVID-19 patients (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3493>)

Reviono, Faizal Muhammad, Ken Zuraida Maharestri, Ihsan Hanif, Coana Sukmagautama, Hendrastutik Apriningsih, Arif Zuhail Amin Hananto, Harsini

Online First: Oct 4, 2022 |

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REVIEW

Mechanism of oxidative stress in obesity (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3849>)

Gede Eka Rusdi Antara, Sri Maliawan

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REVIEW

Comparison of sperm parameters and fertility rate in subclinical varicocele patients treated with varicocelectomy versus no varicocelectomy: a systematic review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3685>)

Afdal, Fakhri Zuhdian Nasher

Online First: Sep 8, 2022 |

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REVIEW

Clostridium difficile virulence factors as the cause of antibiotic-associated diarrhea (AAD): a literature review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3696>)

Ni Luh Putu Harta Wedari, Ni Nyoman Sri Budayanti, Agus Eka Darwinata

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REVIEW

Spine vascular lesions from embryology to imaging findings review article with serial cases (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3812>)

Sri Andreani Utomo, Abdul Hafid Bajamal, Yuyun Yueniwati P.W.

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REVIEW

Benefits and challenges of peer learning methods in health professional students: A literature review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3755>)

Dyah Sriwigati, Lisa Musharyanti

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REVIEW

Behavioral intervention on nonpharmacological pain management for child : a systematic review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3531>)

Wesiana, Ugrasena, Yuni Sufyanti, Nur Hidayah, Resti Utami

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REVIEW

The use of telemedicine in COVID-19 pandemic era: a systematic review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3594>)

Dwi Martha Nur Aditya, Viskasari Pintoko Kalanjati, Dimas Bathoro Bagus Pamungkas, Maya Rahmayanti Syamhadi, Jesslyn Angelina Soegiharto Wibowo, Kevin Muliawan Soetanto

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REVIEW

Medicinal Plants - A Promising Breakthrough in the Management of Alzheimer's Disease Progression Compared to NSAID: A Systematic Review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3899>)

Paulus Sugianto, Widiana Ferriastuti, Kiking Ritarwan, Dwi Putri Rahayu Tampubolon

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REVIEW

Comparison between mini-Percutaneous Nephrolithotomy (PCNL) and standard PCNL in pediatric patients: a systematic review and meta-analysis (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3563>)

Kindy Aulia, Widi Atmoko, Ponco Birowo, Nur Rasyid

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REVIEW

Inflammation in obesity: a review (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3850>)

Tjokorda Istri Anom Saturti

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REVIEW

COVID-19 emergency response in Southeast Asian region: A bibliographic analysis using VOSviewer software (<https://www.balimedicaljournal.org/index.php/bmj/article/view/3758>)

Ferry Fadzlul Rahman, Fahni Haris

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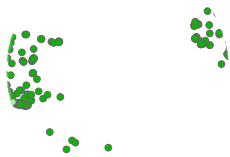


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


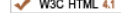

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Medicinal Plants - A Promising Breakthrough in the Management of Alzheimer's Disease Progression Compared to NSAID: A Systematic Review



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Orcid ID: 000-0002-6450-7586

Received: 2022-10-14

Accepted: 2022-11-18

Published: 2022-12-21

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ABSTRACT

Treatment of Alzheimer's Disease is currently limited only to slowing the progression of the symptoms, not curing the disease. Current FDA-approved therapies such as Donepezil, Tacrine, Galantamine, Rivastigmine, and Memantine have quite disturbing side effects, as well as the mechanism of action of these drugs, which is dominated by working as AChE inhibitors. On the other hand, the hypothesis for Alzheimer's causes is varied. Another study also states that Non-Steroid Anti-Inflammatory Drugs (NSAIDs) can be given to people with Alzheimer's. However, the reports were conflicting as one study stated that NSAIDs can help reduce the risk of Alzheimer's; on the contrary, other studies have argued that giving NSAIDs to people with Alzheimer's is not necessary. Despite administering Alzheimer's drugs and NSAIDs, which have adverse side effects on long-term use and high doses, the administration of traditional medicines and medicinal plants can be a good solution due to lower side effects than common drugs, less risk, easy access and affordable. These medicinal plants have several mechanisms to counter the hypothesis that causes Alzheimer's disease.

Keywords: Alzheimer disease, Herbal medicine, NSAID, Medicinal plant.

Cite This Article: Sugianto, P., Ferriastuti, W., Ritarwan, K., Tampubolon, D.P.R. 2022. Medicinal Plants - A Promising Breakthrough in the Management of Alzheimer's Disease Progression Compared to Than NSAID: A Systematic Review. *Bali Medical Journal* 11(3): 1982-1986. DOI: 10.15562/bmj.v11i3.3899

INTRODUCTION

Mild to severe dementia and challenging to recognize, memory failure or Mild Cognitive Impairment (MCI), which slowly becomes severe, and disabling the sufferer, are signs of Alzheimer's Disease (AD).¹ This AD's symptoms are followed by several supporting findings, such as confusion and associated complications, language disturbances, visual complaints, agitation, withdrawal and hallucinations. Symptoms such as Parkinson's disease, increased muscle tone, myoclonus, incontinence and mutism can also occur. In conditions of initiation, malnutrition and pneumonia can result in general death. The AD range lasts from one to 25 years, with the typical clinical duration of the disease 8 to 10 years.²

Overproduction and impaired clearance of β -amyloid is thought to cause AD. Tau hyperphosphorylation and

neuronal toxicity are end events that can be seen. In the blood vessels in the brain, β -amyloid deposits are also found.³ In addition, regarding the presence of A β plaque and NFT, evidence of sustained inflammatory response was also found in the brains of patients with AD. Observational and epidemiological studies in the 1990s demonstrated a protective quality against AD's development with the use of anti-inflammatory drugs in patients with diseases such as rheumatoid arthritis, with a 50% reduced risk of developing AD in patients treated with long term Non-Steroid Anti-Inflammatory Drugs (NSAIDs).⁴

Activation of microglia increases the number of pro-and anti-inflammatory cytokines that regulate the body's immune response due to the TREM2 mutation and other changes in microglial receptors. These cytokine-related changes have been a significant part of evaluating the presence

of AD. The specific cytokines signaling in AD are TNF- α , IL-1 β , IL-6, NFkB, IL-10 dan TGF- β 1.⁴

The current Alzheimer's therapy process focuses on cholinesterase inhibition which limits the enzyme acetylcholinesterase (AChE), which increases acetylcholine in the brain. This cholinesterase inhibition process can be found in the drugs donepezil, tacrine, galantamine, rivastigmine, and memantine.⁵ The drugs used are known to have side effects that are quite uncomfortable; hence it provides potential in alternative medicine using traditional plants. It is known that many traditional plants can improve brain function, but this still needs to be proven empirically due to limited time and sufficient resources.⁶

In traditional medicinal plants, bioactive compounds such as tannins, lignans, polyphenols, flavonoids, sterols, triterpenes, and alkaloids have

the potential to overcome problems related to anti-amyloidogenic, anti-inflammatory, anticholinesterase, hypolipidemic and antioxidant effects.⁵ Antioxidant derivatives that function as neuroprotection protect various components of the nervous system in various ways and positively impact the prevention of Alzheimer's disease.⁷

Many studies have shown that the anti-inflammatory activity of herbal extracts and herbal-derived compounds is mainly due to the inhibition of the metabolism of arachidonic acid (AA), cyclo-oxygenase (COX), lipo-oxygenase (LOX), pro-inflammatory cytokines, nitric oxide, and transcription activation factor (NF- κ B). Several anti-inflammatory medicinal plants are reported to stabilize the lysosomal membrane, and some cause the release of oxidative phosphorylation from intracellular signaling molecules. Many have also been shown to have strong anti-oxygen radical activity.⁸

MATERIALS AND METHODS

ProQuest, JSTOR, PubMed and ScienceDirect are used in this review. The material collection was carried out from February to March 2021 using keywords adjusted to the Medical Subject Heading (MeSH) and Boolean operators (AND, OR NOT or AND NOT) to expand or specify the search. The research method used was PRISMA guidelines followed by literature exclusions. Due to the lack of sources from the literature searched, the keywords specified were "HERBAL" AND "NSAIDs" AND "ANTIOXIDANT" AND "ALZHEIMER".

The inclusion criteria in this literature search were medicinal/traditional plants, human samples, literature from 2015-2021, and Alzheimer's Disease, while the exclusion criteria in this review were if there was discontinuity/irrelevant topic between the abstract and the review material, incomplete literature (not open access), animal samples, non-research literature and other reviews.

RESULT

From the 4 databases, a total of 49 pieces of literature were obtained, which were then reviewed and screened based on

inclusion and exclusion criteria resulting in 13 papers to be reviewed which can be seen in **Figure 1**.

The literature search yielded several papers, including reviews, experimental in vivo, vitro and in-silico (**Table 1**). Particularly, interesting findings were obtained from the in-silico studies. Anti-AD compounds were reported to be the major compound in medicinal plants, with some harboring anti-inflammatory properties. Specific studies in *G. biloba* also yielded promising anti-AD substances which involve the effect toward hormone sensitivity, improvements in endocrine homeostasis, maintenance of endothelial microvascular integrity, and proteolysis of tau protein. Also, a study in *S. miltiorrhiza* yielded potential components such as rosmarinus acid, magnesium lithospermate β , salvianolic acids A, B, and C, and KK's.

Two in-vitro study provided a glimpse of the mechanistic effects of medicinal plant extract in AD. *Malva parviflora*'s extract was capable of inhibiting NF κ B activity in neuroinflammation induced by LPS. In depth analysis reveal that daucosterol was found within the extract which could explain the NF κ B inhibiting effect of the

extract. Another study using *Zingiber monotonum* cystein glycoprotein (ZCPG) extract also yielded a positive effect in terms of AD treatment. ZCPG was proven to be a potent inhibitor of NO $_x$, ROS, and pro-inflammatory cytokines production in lipopolysaccharide-stimulated THP-1 macrophages. Since neuro-inflammation mediated by macrophages or microglia is one of the central pathogenesis in AD, the properties provided by both plant extracts could be potential anti-inflammatory alternatives for AD treatment.

Overall, the ability of natural products to provide anti-amyloid effects is mainly attributed to the inhibition of inflammation of the nerves by natural products. The natural anti-inflammatory product Apigenin affects APP processing and prevention of A β load through downregulation of BACE1 levels, reduced deposition of A β , and decreased insoluble A β levels.⁹

DISCUSSION

The exact cause of Alzheimer's disease is still unclear, but from several studies, it can be concluded that the hypothesis which has been known to trigger

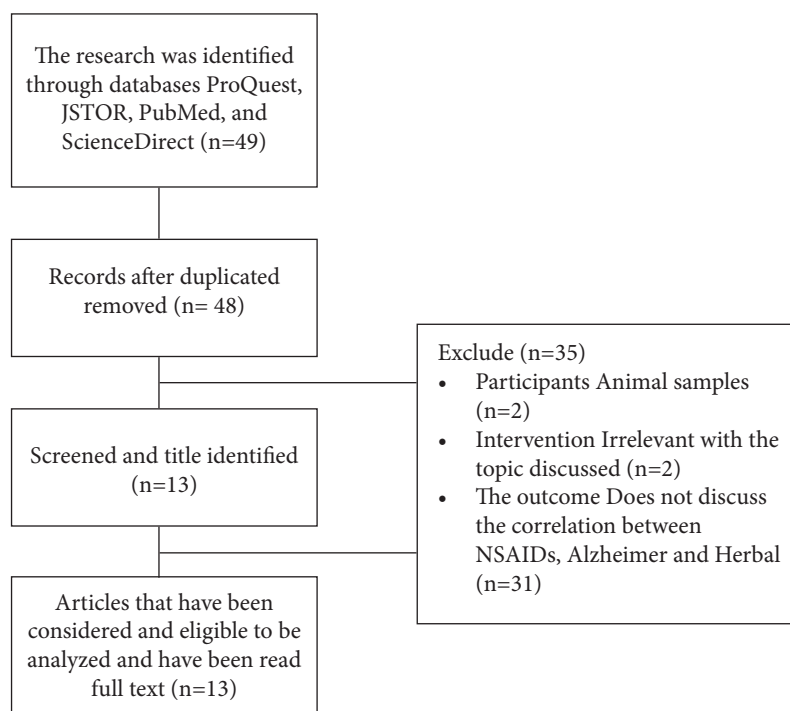


Figure 1. PRISMA diagram flow which illustrates the literature selection process in this review.

Table 1. Summary of the Literature Search included in this study.

No	Authors and Years	Study design	Participant/sample	Summary of Result
1	B. Chen, W. Li, G. Wang, et.al.; 2018	In silico	Traditional Chinese medicine, especially <i>Panax</i> and <i>Morus Genera</i>	Anti-AD compounds were found in 17 candidates structurally identical to 14 existing approved drugs, and most have been reported to affect AD positively. There were 11 Anti-AD compounds with favorable properties; 7 of which are found in anti-AD Chinese plants, moreover, 4 compounds left have anti-inflammatory activity, and 1 compound has immunoregulatory Activity. ²⁰
2	Syad, A.N Devi, K.P.; 2015	review	The botanical pharmacology with special reference to anti-Alzheimer's activity of plants and plant-derived compounds.	Several functions have been found by the botanical pharmacology, such as plants as a source of antioxidants, ChE inhibitors, anti-amyloidogenic activities, anti-inflammatory activities, as β -secretase inhibitors, the protective effect of natural compounds against BBB breakdown and α -secretase inhibitors. ²¹
3	H. Li, X. Sun, F. Yu, et.al.; 2018	in silico	<i>Ginkgo biloba L.</i>	The beneficial effects of <i>G. biloba</i> on AD may be contributed by the regulation of hormone sensitivity, improvements in endocrine homeostasis, maintenance of endothelial microvascular integrity, and proteolysis of tau protein, particularly before amyloid β -protein ($A\beta$) plaque Formation. ²²
4	(M. Sharman, G. Verdile, S. Kirubakaran, et.al., 2019)	review	natural anti-inflammatory and oxidative stress-related	Natural compounds and phytomedicines represent antioxidant, anti-inflammatory, anti-amyloidogenic and neuroprotective effects. Phytonutrients in spices, fruits and vegetables may represent the ideal candidates as they attenuate plaque and tangle formation; decrease neuroinflammation, oxidative and carbonyl stress; and are likely to be safe for long-term treatments at the presymptomatic/ clinical stages of the disease. ²³
5	M. Kamran, R. Kousar, S. Ullah, et.al.; 2020	review article	There were 31 medicinal plants used for Alzheimer's Disease treatment	The alkaloids, flavonoids, and phenolic acids, plants' secondary metabolites, play a crucial role in regeneration improvement and/or neurodegenerative inhibitors. Moreover, the plants which belong to the same taxon share common pharmacological features. ²⁴
6	(Habtemariam, S., 2018)	review	<i>Rosmarinic</i> and <i>Salvianolic acids</i>	<i>Salvianolic acid</i> and <i>Rosmarinic</i> have been proven to target not only AD's biochemical mechanism but also affect the CVD related to stroke. ²⁵
7	I. Mendonça, M. Aurelio, D. Freire, et.al.; 2019	review article	<i>Curcuma longa</i>	Neurotoxic and behavioral damages of in vivo, in vitro, and in vivo-in vitro models of AD were reversed by the curcumin supplementation. ²⁶
8	P. Paudel, S. Seong, Y. Zhou, et.al.; 2018	in silico	<i>Kangen-Karyu</i> and its constituents	proposed a system of activity by which the hydrophobic, π -activity, and hydrophilic associations of salvianolic corrosive B at ATP and substrate destinations are basic for the noticed GSK-3 β restraint. The root of <i>S. miltiorrhiza</i> and its constituents, likewise Rosmarinus acid, magnesium lithospermate β , and salvianolic acids A, B, and C, are KK's active components to inhibit the GSK-3 β . ²⁷
9	Ramirez-Serrano, Cristina; Jimenez-Ferrer, Enrique; Herrera-Ruiz, Maribel; et.al.; 2019	in vitro	<i>Malva parviflora</i> 's fraction	MpF10 fraction could fix the spatial learning and memory impairment and decrease the astrogliosis production in neuroinflammation of the murine model, which is mediated by LPS. Moreover, the <i>daucosterol</i> (MpDau), which prevented LPS-induced neuroinflammation, was found in MpF10; surprisingly, the NF κ B activity in macrophages exposed to LPS was inhibited by both MpF10 and MpDau; hence, the MpF10 is suggested as the new alternative in neuroinflammation treatment such as AD. ²⁸
10.	B. Ahamd, N. Hafeez, A. Rauf, et.al.; 2021	review	<i>Phyllanthus emblica</i>	This plant has memory-enhancing, respiratory, skin and ophthalmic effects and detoxification; furthermore, the biomolecular level study also revealed the potential use of this plant in disease management and control. ²⁹
11	K. Jamir, R. Ganguly, K. Seshagirirao; 2020	in vitro	<i>Zingiber monotonum</i> cystein glycoprotein (ZCPG)	The production of Nitric Oxide, Reactive Oxygen Species and Pro-Inflammatory cytokines in lipopolysaccharide-stimulated THP-1 macrophages was inhibited by the ZCPG, while the production of IL-10 and anti-inflammatory cytokines rose. ³⁰
12	E. Shayganni, M. Bahmani, S. Asgary, et.al; 2016	review	anti-inflammatory plants and their action mechanism and its treatment	Medical plants' active ingredients could inhibit several inflammatory disease symptoms. The free radicals tend to increase along with age and worsen the age-related metabolic disorders. ³¹
13	S. Ahilya, R. Ritesh, M. Gerald; 2021	review	Australian plants' anti-inflammatory compounds	There were cytokines-suppressive anti-inflammatory (CSAIDs) components found in a group of anti-inflammatory which inhibit many pro-inflammatory cytokines expressions like IL-1, TNF- α , and NO; moreover, it targets the pro-inflammatory API. ³²

Alzheimer's disease is the AD Causative hypothesis related to the Tau hypothesis, the Amyloid Cascade hypothesis, which consists of the formation of Amyloid Beta, processing of APP, and Biochemistry of Senile plaques, Cholinergic hypothesis, Oxidative stress hypothesis related to mitochondrial respiration and aggregation of amyloid beta, inflammation hypothesis which also discusses microglia-related pathways, amyloid plaques that produce pro-inflammatory cytokines, and mitochondrial cascade hypothesis which discusses amyloid beta accumulation, formation of NFT and degeneration of synapse in AD.¹⁰

Apart from the unclear cause of Alzheimer's, there is no therapy to cure it. Current therapies are only for slowing down the severity of symptoms of Alzheimer's, some of the drugs that the FDA has approved are Donepezil, Rivastigmine, Galantamine, Memantine and Tacrine. These FDA-approved drugs mostly work as AChE inhibitors for Donepezil, Rivastigmine, Galantamine and Tacrine, while memantine works as a Glutamate overproduce's effects blocker.^{11,12}

Despite the five Alzheimer's drugs in circulation mentioned above, the administration of NSAIDs is also currently known to impact Alzheimer's disease. Current evidence suggests a significantly reduced risk of AD with exposure to NSAIDs, particularly in cohort studies with prospective populations. In contrast, aspirin, acetaminophen or NSAIDs instead of aspirin have not been found. Yet, regarding the weakness of the association, caution is needed to interpret it; hence, larger prospective studies are needed to confirm or refute these findings.¹³

Notwithstanding the Alzheimer's drugs and NSAIDs therapy that have been given, patients with cognitive impairment and those diagnosed with AD should not be given NSAIDs because there is no benefit based on existing clinical evidence. Further research is needed with a longer period and a larger sample size to clarify the role of NSAIDs in the administration of NSAIDs for the treatment of Alzheimer's.¹⁴

Furthermore, in several studies cited by Sharma, due to the many side effects such as

nausea, vomiting, loss of appetite, diarrhea and clumsiness, tacrine is no longer used as an Alzheimer's therapy.^{15,16} In patients on Tacrine treatment, blood monitoring is necessary because of this drug's side effects of hepatotoxicity. Moreover, the short half-life of tacrine, as well as the adverse side effects of high doses, makes it necessary to provide a double dose regimen to maintain prolonged therapeutic activity.¹⁷

Insomnia, nausea, loss of appetite, diarrhea, muscle cramps and muscle weakness are side effects of giving donepezil. When given in high doses, low blood pressure, severe vomiting, muscle weakness, severe nausea, breathing problems, and bradycardia can be experienced by patients receiving donepezil therapy. The main side effects of rivastigmine are stomach upset, weight loss, diarrhea, loss of appetite, nausea and vomiting. Irregular breathing, fast or slow chest pain and slow or irregular heartbeat may occur if the patient has overdosed on rivastigmine. The main side effects of galantamine are seizures, severe nausea, stomach cramps, vomiting, irregular breathing, confusion, muscle weakness and watery eyes. In contrast, memantine can result in blurred vision, dizziness, rapid weight gain, headache and other unexpected symptoms.^{17,18}

There are several mechanisms that possibly happen regarding the Alzheimer's causative hypothesis, such as AD causative, Amyloid cascade, cholinergic, oxidative stress, inflammation, and mitochondrial cascade. The Alzheimer's commercial drugs which are sold publicly mostly focus on the AChE inhibitors, while the NSAIDs therapy only focuses on the inflammation causative. From the review of the literature collected, it is found that various medical and traditional plants have ingredients that function against the hypothesis of the cause of Alzheimer's disease.

The plants' function has a mechanism of action against the Alzheimer's Disease, such as the source of antioxidant, AChE inhibitors, anti-amyloidogenic activities, anti-inflammatory activities, β -secretase inhibitors, BBB breakdown natural protector, γ -secretase inhibitors, and the newest invention is by inhibiting cytokine-mediated events during inflammation.¹⁹

CONCLUSION

Traditional medicine and medicinal plants can be one of the solutions in Alzheimer's therapy, and it has been proven in both in vivo, in vitro and silico studies. The owned content is multifunctional with the hypothesis of the cause of Alzheimer's. Recent studies even mention that Cytokine-Suppressive-Anti-Inflammation Drugs (CSAIDs) are obtained from natural plants, which may be a replacement therapy for NSAIDs in the future, which have fewer side effects and risks because they are obtained from natural ingredients from traditional plants and medicinal plants.

ACKNOWLEDGMENT

We would like to thank all supervisors and staff who contribute to this article from the Department of Neurology, Radiology, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic Hospital and Medical Faculty of Universitas Sumatra Utara.

FUNDING

The authors received no financial support for this article's research, authorship, and/or publication.

CONFLICT OF INTEREST

There is no Conflict of Interest in this patient

PROVENANCE AND PEER REVIEW

Not commissioned, externally peer-reviewed

REGISTRATION OF RESEARCH STUDIES

1. Name of the registry: PROSPERO
2. Unique Identifying number or registration ID: CRD42022357936

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