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# Bali Medical Journal (BaliMedJ)

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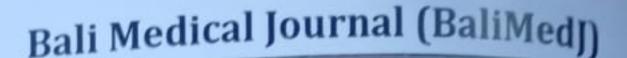
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17-20

20-25



# TABLE OF CONTENTS Volume 10, Number 1, 2021

| 1. | Relationship of gallbladder histopathology towards types of stones in<br>cholelithiasis patients at Universitas Sumatera Utara Hospital, Medan,<br>Indonesia<br>DOI:10.15562/bmj.v10i1.2128   | 1-3  |
|----|---|------|
|    | Adi Muradi Muhar, Denny Rifsal Siregar, Doddy Prabisma  |      |
| 2. | Successful total correction of Transposition of Great Artery in Surabaya's<br>rural area experience: serial cases<br>DOI:10.15562/bmj.v10i1.2005<br>Heroe Soebroto, Farhan Danisa, Arief Rakhman Hakim  | 4-7  |
| 3. | Single Umbilical Artery (SUA) - prenatal sonography diagnosis and vascular<br>imaging features postnatal cord: a case report<br>DOI:10.15562/bmj.v10i1.2024<br>I Nyoman Hariyasa Sanjaya, Cokorda Istri Mirayani Pemayun, Ni Wayan Dewi Purwanti, | 8-10 |

Made Diah Vendita Sakuntari, Ni Putu Nining Gianni, Ni Luh Made Diah Mas Cahyani Putri, Ni Komang Anik Pirgantari, Ni Luh Md Dwi Laxmi Satriani, Firsta Sesarina Mintariani, Ni Luh Putu Yulia Padmawati, Anak Agung Wahyu Putri

- 5. Mean pulmonary artery diameter in chest CT scan in the Thai population ...... DOI:10.15562/bmj.v10i1.1833 Sitang Nirattisaikul, Nuttapat Sunpech, Keerati Hongsakul

| 7.  | A 3-days old infant with neonatal soft tissue sarcoma: a case report<br>DOI:10.15562/bmj.v10i1.2104<br>Dwi Feris Sidabutar, Agung Aji Prasetyo   | 26-29 |
|-----|--|-------|
| 8.  | Vitamin D Receptor (VDR) Apa1 gene polymorphism increasing the risk of<br>breast cancer women in Bali, Indonesia<br>DOI:10.15562/bmj.v10i1.2113<br>I Putu Gede Fajar Mahayasa, I Ketut Widiana, Putu Anda Tusta Adiputra,<br>I Wayan Sudarsa   | 30-34 |
| 10. | Right hepatic artery pseudoaneurysm after choledocoduodenostomy:<br>a case report<br>DOI:10.15562/bmj.v10i1.2106<br>Erik Prabowo, Ahmad Fathi Fuadi, Antonius Gunawan Santoso  | 35-37 |
| 11. | Functional assessment of operative and nonoperative management in major pelvic<br>fracture at Dr. Moewardi Hospital, Surakarta, Indonesia<br>DOI:10.15562/bmj.v10i1.2116<br>Udi Heru Nefihancoro, Muhamad Muamar, Muhammad David Perdana Putra | 38-42 |
| 12. | Delayed laparotomy and gastric repair in gastric perforation: a case report in<br>the neonatal patient<br>DOI:10.15562/bmj.v10i1.2117<br>Barmadisatrio, Ali Sibra Mulluzi  | 43-46 |
| 13. | Liver resection profile in Prof. dr. R.D. Kandou General Hospital:   |       |

1 -----

47-52

53-57

58-62

| 1-year experience   |
|---|
| DOI:10.15562/bmj.v10i1.2118   |
| Michael Iskandar, Michael Tendean, Toar Deliezer Bram Mambu, Ferdinand Tjandra, |
| Jimmy Panelewen, Celine Martino   |

- 14. Sexual satisfaction of Indonesian women with breast cancer in Central Java, Indonesia DOI:10.15562/bmj.v10i1.2119 Yan Wisnu Prajoko, Tommy Supit
- 15. Fractional erbium: YSGG laser compared to the combination of fractional erbium: YSGG laser and topical autologous platelet-rich plasma for treatment of atrophic acne scars: a case report.... DOI:10.15562/bmj.v10i1.2240 Prasetyadi Mawardi, Adniana Nareswari

|     | The role of cholelithiasis risk factors in stone types in cholelithiasis patients at   |       |
|-----|--|-------|
|     | tut tacis risk factors in stone types in   | 63-65 |
| 16  | The role of cholelithiasis risk factors in store 77<br>Universitas Sumatera Utara Hospital<br>Universitas Sumatera V10i1.2139  |       |
| 10  | Universitas Sumatera Utara 1103prese   |       |
|     | DOI:10.15562/bmj.v10i1.2139  |       |
|     | Universitas Sumatere Control Operation Sumatere Control Operation Sumatere Control Operation States Sumatere Control Operation States S |       |
|     | Denny Rifsal Siregar, Add Martan Parts<br>Characteristics of non-genital warts in the dermato-venereology department of<br>he Bedung General Hospital during in 2019   |       |
|     | Characteristics of non-genital warts in the dermato-venercore grant and a Mangusada Badung General Hospital during in 2019   | 66-68 |
| 17. | Characteristics of non- 8<br>Le Bedung General Hospital during in 2019   | 00-08 |
|     | Mangusada Badung General 2038  |       |
|     | DOI:10.15562/bmj.v10i1.2038<br>Efbri Chauresia Dalitan, Anak Agung Ari Agung Kayika Silayukti  |       |
|     | Efbri Chauresia Dalitan, Anak Agung Tirreg o   |       |
|     | Intracranial stenosis in patients with post-ischemic stroke: a case-control study  | 69-73 |
| 18. | Intracranial stenosis in patients with post-ischemic of a  | 15    |
| 10, | DOI:10.15562/bmi.v1011.1989  |       |
|     | Rizaldy Pinzon, Andre Dharmawan Wijono   |       |
|     |  |       |
|     | The change of cell biometric and its nucleus on cervical-squamous-epithelial-  |       |
| 19. | The change of cell biometric and its nucleus on each high-risk human papillomavirus cell with GA genotype of Fas-promoter-670 gene, high-risk human papillomavirus   |       |
|     | cell with GA genotype of Fas-promoter-0/0 gene, mg   | 74-81 |
|     | and Candida species infection: a case report   | /4-01 |
|     | DOI:10.15562/bmj.v10i1.2138  |       |
|     | Edy Parwanto, Raditya Wratsangka, Assangga Guyansyah, Kirana Anggraeni,  |       |
|     | Reza Aditya Digambiro, David Tjahyadi, Hanslavina Arkeman, Haryo Ganeca  |       |
|     | Widyatama, Hosea Jaya Edy, Yosua Jaya Edy  |       |
|     |  |       |
| 19  | DNA barcoding in molecular identification and phylogenetic relationship of   |       |
| 1). |  |       |
|     | beneficial wild Balinese red algae, Bulung sangu (Gracilaria sp.)  | 82-88 |

### DOI:10.15562/bmj.v10i1.2093

I Gede Putu Wirawan, Maria Malida Vernandes Sasadara, I Nyoman Wijaya, Anak Agung Keswari Krinandika

20. Video-assisted thoracoscopic surgery in the treatment of empyema: a case series... 89-94 DOI:10.15562/bmj.v10i1.2121 Yustinus Rurie Wirawan, Christotheme, Annal and Annal and Annal and Annal and Annal and Annal A

95-98

99-102

Yustinus Rurie Wirawan, Christophoroes Jonathan Tansil

- 21. Simultaneous resection on the patient with synchronous colorectal liver metastasis: two cases report...... DOI:10.15562/bmj.v10i1.2122 Celine Martino, Michael Tendean, Toar D. B. Mambu, Ferdinand Tjandra, Michael Iskandar
- 22. Correlation of CD44 and CD24 expression with the positive response after neoadjuvant chemotherapy in stage IIIB breast cancer patient at Dr. Saiful Anwar Hospital, Malang, Indonesia..... DOI:10.15562/bmj.v10i1.2123 Muhammad Bachtiar Budianto, Artono Isharanto, Andry Haris

| 23. | Patients' characteristics following reoperation after Modified Blalock-<br>Taussig Shunt (MBTS) in Cardiac Centre National General Hospital<br>Cipto Mangunkusumo from 2018-2020   |         |
|-----|--|---------|
|     | DOI:10.15562/bmj.v10i1.2124<br>Suprayitno Wardoyo, Joshua Parsaoran Partogi Pardede, Hari Agung Asari  | 103-107 |
| 24. | Penile gangrene as a priapism sequele due to Chronic Myeloid Leukemia (CML):<br>the first report in Indonesia.<br>DOI:10.15562/bmj.v10i1.2125  | 108-110 |
|     | Deddy Rasyidan Yulizar, Eka Putri Maulani, Heru Prasetya, Hendra Sutapa,<br>Eka Yudha Rahman   |         |
| 25. | The effects of <i>cyclophosphamide</i> , <i>adriamycin</i> and <i>5-fluorouracil</i> chemotherapy on<br>blood cells and cardiac hemodynamics in breast carcinoma patients: a case study at<br>Dr. Kariadi General Hospital, Semarang, Indonesia<br>DOI:10.15562/bmj.v10i1.2126<br>Sibin Chandra, Djoko Handojo | 111-118 |
| 26. | Radiofrequency ablation for management of thyroid nodules: a case report<br>DOI:10.15562/bmj.v10i1.2150<br>Kristanto Yuli Yarsa, Monica Bellynda   | 119-121 |
| 26. | The future of three-dimensional skin graft: a mini-review<br>DOI:10.15562/bmj.v10i1.2242<br>Zendio Abednego Santoso  | 122-125 |

27. The correlation TNF-α gene promoter region-238G, -308G, -857, and -1031

| polymorphism with psoriasis vulgaris                              | 126-131 |
|---|---------|
| DOI:10.15562/bmj.v10i1.2328                                       |         |
| Cashtri Meher, R. Lia Kusumawati Iswara, Irma D. Roesyanto-Mahadi |         |

29. The role of psychosocial stressors, carbohydrate and protein intake on serum serotonin and cortisol levels in patients with depression: a preliminary evaluation 137-141 DOI:10.15562/bmj.v10i1.2315

Alifiati Fitrikasari, Natalia Dewi Wardani, Tanjung Ayu Sumekar, Fanti Saktini, Hang Gunawan Asikin1, Mohamad Sulchan, I Dewa Made Sukrama

| 30. | COVID-19 vaccination in patients with cancer: Position paper from<br>the Indonesian Society of Hematology and Medical Oncology (ISHMO)  | 142-150 |
|-----|---|---------|
|     | of Semarang<br>DOI:10.15562/bmj.v10i1.2273<br>Eko Adhi Pangarsa, Budi Setiawan, Santosa, Ridho Monotoc Naibaho, Daniel Rizky,<br>Mike Lumban Tobing, Muchlis Achsan Udji Sofro, Catharina Suharti   |         |
|     | E service workstation reduces electrical activity of upper trapel fiber   | 151-155 |
|     | twisting process<br>DOI:10.15562/bmj.v10i1.2187<br>Chandra Dewi Kurnianingtyas, I Putu Gede Adiatmika, Ketut Tirtayasa,   |         |
| 32. | I Wayan Surata<br>The ethanol extract of Garcinia mangostana L peel reduces the isoniazid-induced   | 156-159 |
|     | liver damage in rats<br>DOI:10.15562/bmj.v10i1.2108<br>Triyanta Yuli Pramana, Brian Wasita, Vitri Widyaningsih, Risya Cilmiaty, Suroto,<br>Ambar Mudigdo, Bambang Purwanto  | 150-159 |
|     | Intravenous Wharton's Jelly stem cell increased the number of β cells pancreas<br>and reduced the fasting blood glucose level in diabetes mellitus Wistar rat male<br>( <i>Rattus norvegicus</i> )<br>DOI:10.15562/bmj.v10i1.2306<br>Nadia Permatasari, Wimpie Pangkahila, Anak Agung Gde Budhiarta | 160-163 |

34. Pectoralis major myocutaneous flap for head and neck reconstruction: a case report ..... 164-166 DOI:10.15562/bmj.v10i1.2112 Oktahermoniza, Ari Oktavenra, Daan Khambri Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate the infertile population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia ..... 167 Assangga Guyansyah, Raditya Wratsangka, Denny Dhanardono, Muhammad Farid Ghazali, Hosea Jaya Edy, Haryo Ganeca Widyatama, Dietha Kusumaningrum, David Tjahyadi, Edy Parwanto 3 1.1.1 equation ances the performance of healthcare leaders? A systematic review..... DOI:10.15562/bmj.v10i1.2014 174-18 Awal Prasetyo, Jethro Budiman, Muzakar Isa

| 37. | Management of giant thyroglossal duct cyst in Dr. Moewardi Hospital Indonesia:   |         |
|-----|--|---------|
|     | A case report<br>DOI:10.15562/bmj.v10i1.2111<br>Muhammad David Perdana Putra, Joko Purnomo, Kristanto Yuli Yarso   | 181-183 |
| 38. | Aggressiveness tumor: a case report of recurrent ameloblastoma in the mandible .<br>DOI:10.15562/bmj.v10i1.2114<br>Marjono Dwi Wibowo, Agung Fuad Fathurochman   | 184-188 |
| 39. | Anti-diabetic properties of Stevia rebaudiana Bertoni as sugar substitute:<br>a mini-review<br>DOI:10.15562/bmj.v10i1.2259<br>Yudi Kristanto, Angeline Rosa Hartono  | 189-193 |
| 40. | Comparison of skin hydration degrees based on moisturizing time in children's<br>atopic dermatitis<br>DOI:10.15562/bmj.v10i1.2137<br>Puteri Wulandari, Syahril Rahmat Lubis, Deryne Anggia Paramita  | 194-198 |
| 41. | Acute kidney injury in patient with djenkolism: a case report<br>DOI:10.15562/bmj.v10i1.2146<br>Yenny Kandarini, Made Edwin Sridana, Gede Wira Mahadita  | 199-201 |
| 42. | Evaluation of patient's daily activities with Free Non-Vascularized Fibular Head<br>Graft (FNVFHG) as a treatment after resection of proximal humeral tumors<br>DOI:10.15562/bmj.v10i1.2270<br>Muhammad Phetrus Johan, Henry Yurianto, Roichan Mochammad Firdaus | 202-207 |

|                        | in, menny rananto | , Rotentan Moentantinua | тицииз, |
|------------------------|-------------------|-------------------------|---------|
| Andi Firman Mubarak, L | uky Tandio Putra, | Tri Kurniawan           |         |

| 43. | An overview of overactive bladder<br>DOI:10.15562/bmj.v10i1.2266  | 208-210 |
|-----|---|---------|
|     | I Putu Gde Fredy Gunawan, I Nyoman Suarjana, Kadek Frida Wulandari  |         |
| 44. | Case report of Laryngeal Amyloidosis: Unusual cause of hoarseness<br>DOI:10.15562/bmj.v10i1.1795  | 211-213 |
|     | Noraimi Khamalrudin, Mohd Razif Mohamad Yunus, Marina Mat Baki, Foong Seong Kir   | 1       |
| 45. | The correlation of blood thiamine concentrations with lactate acidosis in peritonitis patients with sepsis.   | 214-218 |
|     | DOI:10.15562/Dmj.v10i1.2237   |         |
|     | Maria Meilita Sinaga, Vicky Sumarki Budipramana, Jusak Nugraha  |         |
| 46. | Use of smartphone-based self-monitoring blood glucose application in type 2<br>diabetes mellitus patients in Indonesia: A pre and post-test study<br>DOI:10.15562/bmj.v10i1.2181<br>Ida Ayu Kshanti, Muhammad Ikhsan Mokoagow, Rulli Rosandi, Marina Epriliawati,<br>Jerry Nasarudin, Nadya Magfira | 219-224 |

|     | <ol> <li>Keloid after orthopedic surgery: prevention, current therapy modalities, and</li> <li>Keloid after orthopedic surgery: prevention, current therapy modalities</li> </ol>   |         |
|-----|---|---------|
|     | lie curgery: prevention, current mer 17   | 225-228 |
| 4   | <ol> <li>Keloid after orthopedic surgery: prevention, current<br/>emerging therapies modalities</li> <li>15562/bmj.v10i1.2264</li> </ol>  | 0       |
|     | emerging therapies moduli 2264  |         |
|     | DOI:10.15502/0229   |         |
|     | Andrew Sutheno  |         |
|     | to a f CD133+ bone marrow stem cell for runder by by pass graft   |         |
| 48  | <ol> <li>A new hope of CD133+ bone marrow stem cell for function</li> <li>A new hope of CD133+ bone marrow stem cell for function graft</li> <li>improvement in low ejection fraction coronary artery bypass graft</li> </ol> | 229-223 |
|     | improvement in low ejection fraction coros a patients: a clinical trial   | -423    |
|     | patients: a childen a<br>DOI:10.15562/bmj.v10i1.2264  |         |
|     | Tri Wisesa Soetisna   |         |
|     | A new hope of CD133+ bone marrow stem cell for functional exercise capacity   |         |
| 49  | A new hope of CD133+ bone marrow stem cell for functional bypass graft  |         |
| 4)  | A new hope of CD133+ bone marrow stem cerror artery bypass graft<br>improvement in low ejection fraction coronary artery bypass graft   | 229-223 |
|     | patients: a clinical trial  | 229-223 |
|     | DOI:10.15562/bmj.v10i1.2264   |         |
|     | Tri Wisesa Soetisna   |         |
|     | 1 have dialysis and hemodialysis with   |         |
| 49  | Blood pressure difference between regular hemodialysis and hemodialysis with  | 234-237 |
|     | hemoperfusion at Haji Adam Malik Hospital, Medan-Indonesia  | 254-25/ |
|     | DOI:10.15562/bmj.v10i1.846  |         |
|     | Dedy Shauqi Fachrianda Situmorang, Alwi Thamrin Nasution, Syafrizal Nasution  |         |
| 50  | The role of epidermal growth factor receptor as progression factor in cervical  |         |
| 50. | intraepithelial neoplasia and squamous cell carcinoma   | 220 242 |
|     | DOI:10.15562/bmj.v10i1.2349   | 238-242 |
|     | I Gusti Ayu Sri Mahendra Dewi, Ni Putu Sriwidyani, Ni Putu Ekawati  |         |
|     | , and Denny In I and Orthing unit, IN I and ERAWALI   |         |
| 51. | Purple sweet potato extract and vitamin C increase the proliferation of endothelial   |         |
|     | Progenitor cens from stable coronary artery disease nationto  | 243-248 |
|     |   | 245-240 |
|     | Luh Oliva Saraswati Suastika, Yudi Her Oktaviono, Djoko Soemantri, Ferry Sandra   |         |
| 50  | Deltante, Dioko Soemanni, Ferry Sanara  |         |
| 52. | Predicting factors for walking ability of postoperative patients with<br>hemiarthroplasty at Wahidin Sudirobused a U  |         |
|     | hemiarthroplasty at Wahidin Sudirohusodo Hospital in Makassar   | 249-255 |
|     | Muhama 10 juli 2256   | 249-255 |
|     | Muhammad Sakti, Ruksal Saleh, Khrisna Yudha, Taufiq Akbar   |         |
| 53. | Correlation 1   |         |
|     | Correlation between nail psoriasis severity index score with quality of life in<br>DOI:10.15562/herei   |         |
|     | nail psoriasis  | 256-260 |
|     |   | 250-200 |
|     | Abdul Arif, Irma Damayanti Roesyanto Mahadi, Ariyati Yosi   |         |
|     | And Williamic of C. J. J.   |         |
|     | in Overnutritions child   |         |
|     | DOI:10.15562/bmi v10:1 or with Dengue Infection Molecule -1 (sVCAM-1) level   | 261-265 |
|     | in Overnutritious children with Dengue Infection Molecule -1 (sVCAM-1) level<br>DOI:10.15562/bmj.v10i1.2304<br>Ni Kadek Elmy Saniathi, Mohammad L. G.   | 201-20  |
|     | Johannad Juffrie, Bambana III   |         |
|     | Ni Kadek Elmy Saniathi, Mohammad Juffrie, Bambang Udji Djoko Rianto, Soetjiningsih  |         |

| 55. | Decision to Delivery Interval in Emergency Cesarean Section at Two Academic<br>Hospitals in Yogyakarta and Central Java, Indonesia<br>DOI:10.15562/bmj.v10i1.2030<br>Shinta Prawitasari, Doni Widyandana, Mohammad Hakimi, Adi Utarini | 266-272 |
|-----|--|---------|
| 56. | Decision to Delivery Interval in Emergency Cesarean Section at Two Academic<br>Hospitals in Yogyakarta and Central Java, Indonesia<br>DOI:10.15562/bmj.v10i1.2030<br>Shinta Prawitasari, Doni Widyandana, Mohammad Hakimi, Adi Utarini | 266-272 |
| 56. | Evaluation of chronic disease management programs in developed and<br>underdeveloped regions in Indonesia<br>DOI:10.15562/bmj.v10i1.2099<br>Ahmad Muhammad Kasim, Yodi Mahendradhata, Laksono Trisnantoro                              | 273-280 |
| 57. | Evaluation of chronic disease management programs in developed and<br>underdeveloped regions in Indonesia<br>DOI:10.15562/bmj.v10i1.2099<br>Ahmad Muhammad Kasim, Yodi Mahendradhata, Laksono Trisnantoro                              | 273-280 |
| 58. | Criteria for palliative care referral in oncology practice:<br>An instrument development<br>DOI:10.15562/bmj.v10i1.2099<br>Maria A Witiaksono Christantia Efferedu Sei Maladrik I  | 281-290 |

Mulatsih, Iwan Dwiprahasto, Adi Utarini

- 59. Correlation of low vitamin D status with atopic dermatitis severity in children ...... 291-295 DOI:10.15562/bmj.v10i1.2203 Habibah Hasyim Lubis, Kristo Alberto Nababan, Deryne Anggia Paramita

Muhammad Ridlo, Imam Budi Putra, Nelva Karmila Jusuf

#### **ORIGINAL ARTICLE**

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Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate the infertile population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia



Assangga Guyansyah<sup>1</sup>, Raditya Wratsangka<sup>1</sup>, Denny Dhanardono<sup>1</sup>, Muhammad Farid Ghazali<sup>2</sup>, Hosea Jaya Edy<sup>3</sup>, Haryo Ganeca Widyatama<sup>4</sup>, Dietha Kusumaningrum<sup>5</sup>, David Tjahyadi<sup>6</sup>, Edy Parwanto<sup>7\*</sup>

#### ABSTRACT

Introduction: Indonesia is a country with a large agricultural and industry, known to utilize various types of pesticides, as well as several other industries with uncontrolled pollution levels distributed across the nation. Besides, numerous studies have stated the adverse effects of chemicals substances used in daily life and industrial waste on the health of living things, including humans. This study aimed to determine the infertility characteristic in the agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia.

**Methods:** The study was conducted retrospectively on medical records. Therefore, this study determined the infertility characteristics based on sperm analysis, the etiology of the causes of infertility in female, and the diagnosis of infertility. Data collection was obtained from patients' medical records in the Infertile Poly of Mitra Bunda Amanda Hospital Karawang, Karawang Regency, West Java Province, Indonesia.

**Result:** The results showed infertility was most prevalent in males aged 30-40 years (55.79%) and females below 30 years (61.05%). Furthermore, the male and female's most prevalent educational qualification (33.68% and 36.84%, respectively) was discovered to be high school diploma. In terms of occupation, most male (56.84%) were laborers, while the female was mostly housewives (36.84%). Meanwhile, oligoasthenoteratozoospermia was the most analyzed sperm type (33.68%), and polycystic ovary syndrome was the most common etiology of infertility in females (26.32%). The most prevalent diagnosis was primary infertility factors, male and female (45.26%).

**Conclusion:** Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate the infertile population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia.

**Keywords:** pollutants, sperm analysis, infertility, oligoasthenoteratozoospermia, polycystic ovary syndrome. **Cite This Article:** Guyansyah, A., Wratsangka, R., Dhanardono, D., Ghazali, M.F., Edy, H.J., Widyatama, H.G., Kusumaningrum, D., Tjahyadi, D., Parwanto, E. 2021. Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate the infertile population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia. *Bali Medical Journal* 10(1): 167-173. DOI: 10.15562/bmj.v10i1.2281

> estrogenic effects generally have biological effects in women, as pollutants with antiandrogenic effects that affect male fertility.<sup>3</sup>

> Pollutants from agricultural and industrial activities can pollute the air, water and soil. Of course, pollutants can move places. Pollutants in the air can move to water and land or vice versa. Directly or indirectly, pollutants can cause human health problems. Air pollution

can occur because it contains particles with aerodynamic diameters below 10 and 2.5  $\mu$ m (PM10 and PM2.5). Apart from that, it can also contain NO, NO2, NOx and SO2. It has been proven that air pollutants cause endocrine disorders and hormonal disturbances. Women exposed to high concentrations of air pollutants, namely PM 2.5, NO, NO2, NOx and SO2, have a high risk of developing polycystic

<sup>1</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Trisakti, Indonesia. <sup>2</sup>Polyclinic of Infertil, Mitra Bunda Amanda Karawang Clinic, Karawang Regency, West Java, Indonesia <sup>3</sup>Program Study of Pharmacy, Faculty of Math and Natural Sciences, Universitas Sam Ratulangi, Indonesia <sup>4</sup>Medical doctor of Bhakti Mandala Clinic, Tangerang Regency, Banten Province, Indonesia.

<sup>5</sup>Medical doctor of Batari Husada Clinic, Duren Sawit, East Jakarta, Special Capital Region of Jakarta, Indonesia <sup>6</sup>Department of Histology, Faculty of Medicine, Universitas Trisakti, Indonesia. <sup>7</sup>Department of Biology, Faculty of Medicine, Universitas Trisakti, Indonesia.

\*Corresponding author: Edy Parwanto; Department of Biology, Faculty of Medicine, Universitas Trisakti, Indonesia; edyparwanto@trisakti.ac.id; edy.parwanto@gmail.com

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#### **INTRODUCTION**

Pollutants are harmful to human health and damage the environment. Pollutants in the human environment have various effects that are detrimental to health to cause disease.<sup>1</sup> The character of disease risk due to exposure to multi-pollutants can be determined using an "environmental risk score".<sup>2</sup> Environmental pollutants with ovary syndrome.<sup>4</sup> Besides that, it has been shown that particles less than 0.3  $\mu$ m in diameter can dominate the acute effects of particulate air pollution resulting in cardiac autonomic dysfunction.<sup>5</sup>

Furthermore, it was reported that PM interferes with energy metabolism, thereby disrupting the endocrine glands and becoming a risk for cardiovascular disease.<sup>6</sup> In this regard, we have reported a case of aortic enlargement on the cadaveric heart and great vessel dimensions.7 Because that, studies are still needed on the effect of pollutants on aortic enlargement. That is important because cardiovascular disease as a risk factor has been shown to have a strong correlation with a history of infertility in women of childbearing age and menopause.8 Moreover, chemicals used in the textile industry are believed to produce persistent organic pollutants These chemicals include (POPs). dichlorodiphenyltrichloroethane (DDT), dichlorodiphenyldichloroethylene (p,p'-DDE) and polychlorinated biphenyls (PCBs). POP is a stable lipophilic compound found in the environment. These pollutants are difficult to break down, insoluble in water, and accumulate in the human body. Furthermore, pollutants in the body can cause human health problems.9 How are people living in agricultural and industrial areas exposed to pollutants?.

Of course, people living in the area are exposed to various pollutants from agricultural and industrial activities. One proof that agricultural and industrial activities in Karawang Regency, West Java Province, Indonesia, impact the environment can be seen in the water quality of the Citarum river. The Citarum River is a large and long river in West Java that crosses Karawang Regency. It has been reported that the water in the Citarum river is of poor quality, making it unsuitable for drinking. This fact illustrates that the water in the Citarum river contains high pollutants.<sup>10</sup> It should be noted that 18 sub-districts in Karawang Regency are crossed by the downstream segment of the Citarum River. Furthermore, it is shown that the high pollutant load of COD, BOD, phosphate and nitrate in the downstream section of the Citarum river. The high pollutant load found in the Citarum river

| Age         | N (190 Subjects) | %      |  |  |  |  |  |
|-------------|------------------|--------|--|--|--|--|--|
| Male        | 95               |        |  |  |  |  |  |
| <30 years   | 35               | 36.84% |  |  |  |  |  |
| 30-40 years | 53               | 55.79% |  |  |  |  |  |
| >40 years   | 7                | 7.37%  |  |  |  |  |  |
|             |                  |        |  |  |  |  |  |
| Female      | 95               |        |  |  |  |  |  |
| <30 years   | 58               | 61.05% |  |  |  |  |  |
| 30-40 years | 35               | 36.84% |  |  |  |  |  |
|             |                  |        |  |  |  |  |  |

2

#### Table 1. Age distribution of Research Subjects

#### Table 2. Educational qualification of Research Subjects

>40 years

| Age                | N (190 Subjects) | %      |
|--------------------|------------------|--------|
| Male               | 95               |        |
| Junior High School | 20               | 21.05% |
| High School        | 32               | 33.68% |
| Academy            | 25               | 26.32% |
| Bachelor           | 18               | 18.95% |
| Female             | 95               |        |
| Junior High School | 30               | 31.58% |
| High School        | 35               | 36.84% |
| Academy            | 22               | 23.16% |
| Bachelor           | 8                | 8.42%  |

#### Table 3. Characteristics of Research Subjects Based on Occupation

|                   | •                | •      |
|-------------------|------------------|--------|
| Age               | N (190 Subjects) | %      |
| Male              | 95               |        |
| Laborer           | 21               | 22.11% |
| Factory Employees | 54               | 56.84% |
| Entrepreneur      | 28               | 29.47% |
| Civil servants    | 12               | 12.63% |
|                   |                  |        |
| Female            | 95               |        |
| Laborer           | 12               | 12.63% |
| Factory Employees | 22               | 23.16% |
| Entrepreneur      | 18               | 18.95% |
| Civil servants    | 12               | 12.63% |
| Housewife         | 35               | 36.84% |
|                   |                  |        |

downstream is caused by excess waste from domestic, agricultural and industrial activities.<sup>11</sup>

Epidemiological studies show that pollutants affect animal and human life. It has been shown that air pollution plays a role in infertility. Factory waste is a disruptive endocrine hormone able to damage the body's endocrine system through various mechanisms.<sup>12</sup> Moreover that pollutants disrupt spermatogenesis, leading to decreased reproductive capacity in exposed populations.<sup>13</sup> The results of previous studies show the effect of environmental lead pollution on blood lead and sex hormone levels in the electronic waste disposal area.<sup>14</sup> Previous studies have also shown that pollution affects chromosomes, thereby affecting infertility and sex hormone levels.<sup>15</sup> Infertility is still a problem for many married couples. It was also stated that the average age of childbearing in women was increasing.<sup>16</sup> Moreover that infertility in Indonesia occurs in about 10-15% of couples of childbearing age.<sup>17</sup>

2.11%

Based on the researchers' data, it is necessary to conduct a study on the

characteristics of infertile communities living in agricultural and industrial areas. The purpose of this study was to determine the characteristics of infertility in agricultural and industrial areas. The infertility characteristics include the results of sperm analysis, the etiology of the causes of infertility in females, and the diagnosis of infertility in the agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia.

#### **METHODS**

This research is a retrospective study with descriptive analysis. This research is part of a research project on infertility characteristics in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia, in 2015-2020.

The research material is secondary data obtained from the medical records of patients. The study was conducted from June to November 2019 in the Infertile Poly of RSIA Mitra Bunda Amanda Karawang, Karawang Regency, West Java Province, Indonesia. Collection of medical record data used from January 1<sup>st</sup> to December 31<sup>st</sup> 2015. The individuals whose data were used in this study all live in Karawang Regency, West Java, Indonesia.

#### RESULTS

Based on the Table 1, showed infertility was most prevalent in males between 30 and 40 years (55.79%), followed by the age group below 30 years (36.84%) and above 40 years (7.37%). Meanwhile, in the female, infertility was most prevalent in the age group below 30 years (61.05%), followed by female aged 30-40 years (36.84%), and above 40 years (2.11%).

According to Table 2, the most common educational qualification possessed by male education is high school diploma (33.68%), followed by the academy (26.32%), junior high school (21.05%), and bachelor (18.95%) degrees. Similarly, the most prevalent educational qualification possessed by the female was high school diploma (36.84%), followed by junior high school (31.58%), academy (23.16%), and bachelor (8.42%) degrees.

Based on Table 3, infertility was discovered to be most prevalent in

| Table 4. | Infertility diagnosis based on the research Subject | ts |
|----------|---|----|
|          |   |    |

| Diagnosis                                      | (N=95 couples) | %      |
|--|----------------|--------|
| Primary Infertility ex Male Factor             | 30             | 31.58% |
| Primary Infertility of Male and Female Factors | 43             | 45.26% |
| Primary Infertility ex Female factor           | 18             | 18.95% |
| Secondary Infertility                          | 4              | 4.21%  |

#### Table 5. The Etiology of Infertility in the Female Research Subjects

| Etiology      | N (95 Subjects) | %      |
|---------------|-----------------|--------|
| Tubal Factor  | 19              | 20.0%  |
| PCOS          | 25              | 26.32% |
| Myoma         | 16              | 16.84% |
| Endometriosis | 20              | 21.05% |
| Ovulation     | 15              | 15.79% |

Abbreviations: PCOS=polycystic ovary syndrome

| Ta | ble 6 | . S | perm | Ana | lysis | of | Resear | ch S | Subj | ects |
|----|-------|-----|------|-----|-------|----|--------|------|------|------|
|----|-------|-----|------|-----|-------|----|--------|------|------|------|

| Age                          | N (95 Subjects) | %      |
|------------------------------|-----------------|--------|
| Normospermia                 | 4               | 4.21%  |
| Oligospermia                 | 6               | 6.32%  |
| Asthenospremia               | 4               | 4.21%  |
| Teratospermia                | 7               | 7.37%  |
| Oligoasthenospremia          | 20              | 21.05% |
| Oligoteratozoospremia        | 22              | 23.16% |
| Oligoasthenoteratozoospermia | 32              | 33.68% |

factory employees (56.84%), followed by entrepreneurs (29.47%), laborers (22.11%), and civil servant males (12.63%) in terms of occupation. Meanwhile, in the female, infertility cases were most prevalent in housewives (36.84%), followed by factory employees (23.16%), laborers (12.63%), and civil servants (12.63%).

Based on Table 6 shows the most common infertility diagnosis was primary infertility male and female factor (45.26%), followed by primary infertility ex male factor (31.58%), primary infertility ex female factor (18.95%), and secondary infertility (4.21%).

According to Table 5, the etiology of infertility in females was discovered to be majorly due to polycystic ovary syndrome (PCOS), 26.32%, followed by endometriosis 21.05%, tubal factors 20.0%, myoma 16.84%, and ovulation 15.79%.

Based on Table 6 shows that oligoasthenoteratozoospermia being the most prevalent sperm type (33.68%), followed by oligoteratozoospermia (23.16%), oligoasthenospermia (21.05%), teratospermia (7.37%), oligospermia (6. 32%), normospermia (4.23%), and asthenospermia (4.23%).

#### DISCUSSION

This study showed that infertility is most prevalent in males between 30 and 40 years (55.79) and females below 30 years (61.05%). Ordinarily, these age groups ought to be rather reproductive. However, on the contrary, these are the groups with the most infertility problems. Meanwhile, the highest educational qualification possessed by the male and female is High School diploma (33.68% and 36.84%, respectively). That is a possible early indication of the factories' harmful impact in work environments and around residences. It has been reported that demographic factors such as gender, education, income and geographic location influence the prevalence of infertility in infertile Chinese men and women.<sup>18</sup> Besides, the general levels of education, knowledge, and socioeconomic development within the region are currently low. Consequently, many people

are ignorant or forced to live near factories and to utilize polluted water sources. In terms of occupation, the males were mostly laborers (56.84%), while the female was mostly housewives (36.84%). The occupation of laborers is a possible cause of infertility, especially in exposure to heat and direct contact with heat sources, often encountered in the manufacture of the metal rim, tires, steel plates, zinc, machine operators, motorcycle body frames, forklifts, and other products. This exposure of male reproductive organs to heat is possibly associated with reduction in sperm quality. That can occur because high temperatures cause an increase in testicular metabolism so that sperm is damaged.19

Pollution has detrimental effects on health, not only by direct inhalation of pollutants but also through other means of exposure, including ingesting contaminated water or skin contact. One easy example is carbon monoxide as a pollutant from industrial activities. In humans, carbon monoxide poisoning affects the cardiovascular, neurological, and affective systems.<sup>20</sup> The most common health effects are respiratory infections. However, pollutants affect all body systems, including reproduction. The exact pathophysiology of the pollutant effect on ovaries is not currently known. However, pollutants bind to hemoglobin during blood circulation and cause toxicity upon entering body organs.<sup>21</sup> We already know that agricultural and industrial activities produce pollutants as a by-product. Therefore the negative effects of pollutants on the population must be avoided. Also, the government has long-established technical guidelines for industrial estates (Pedoman Teknis Kawasan Industri).<sup>22</sup>

Based on the diagnosis of infertility, this study showed that the main factor of male and female infertility has the biggest role compared with the other factors (Table 4). We already know that various hormones play a role in the reproductive process, including gonadotrophinreleasing hormone (GnRH), folliclestimulating hormone (FSH), luteinizing hormone (LH), estrogen, progesterone, testosterone, and inhibin. It has been proven that estrogen plays a role in the reproductive system of women and men.

Apart from that, estrogen also plays a role in the neuroendocrine, skeletal, vascular and immune systems. Therefore, estrogen has implications for infertility and other diseases.<sup>23</sup> Therefore, exogenous estrogenic compounds have the potential to interfere with the reproductive system. In this regard, the effects of diethylstilbestrol (DES) and methoxychlor (MXC) have been investigated on female rhesus monkeys' peripubertal period. These studies' results indicate that DES had a striking effect on adolescent maturation, and MXC also altered development during this period. The pattern of effects across agents and doses may be based on specifics of estrogenic action.<sup>24</sup> On the other hand, it has also been proven that xenoestrogen is involved in the decrease in the number and quality of human sperm, consequently contributing to a decrease in fertility and decline in the proportion of male births. Xenoestrogens have also been shown to increase the occurrence of abnormalities in the male reproductive tract. Moreover, it has also been shown that xenoestrogens play a role in increasing spontaneous abortion.25

It has been stated that primary infertility is associated with protein that binds with sex hormones. In humans, some proteins bind with sex hormones in the circulatory system and the testes. The protein that binds with sex hormones in the circulating system is called sex hormone-binding globulin (SHBG). Proteins that bind to sex hormones in the testes are called androgen binding proteins (ABP). SHBG in the circulatory system has a function to bind sex steroid hormones and mediate the work of these hormones to target cells outside the testes, while ABP functions to mediate the action of sex steroid hormones in the testes.<sup>26</sup> It is shown that the distribution of SHBG concentrations is broad-based on age and body mass index (BMI) values in primary infertile men. From these two variables, it turns out that the relationship between BMI and a decrease in SHBG levels is stronger than the relationship between age and increased levels of SHBG.27 The other study showed that the levels of SHBG, total testosterone, free testosterone and percent of free testosterone have a negative correlation with age, but the

insulin and free testosterone index do not correlate with age. The decrease in SHBG levels per decade in healthy Indonesian men was 8.19%, while the decrease of total testosterone levels per decade in healthy Indonesian men was 9.8%.<sup>28</sup> The results of previous studies show that low total testosterone levels can increase fasting blood glucose levels in adult men, but SHBG levels do not predict fasting blood glucose levels.<sup>29</sup> Although it has been stated that SHBG levels are influenced by many factors, including genetic factors such as the genetic polymorphism of SHBG.<sup>30</sup>

Research has been carried out concerning primary infertility to reduce SHBG levels in postmenopausal women, namely by isoflavone supplementation.<sup>31</sup> We recommend that this method be implemented in women of childbearing age to increase fertility. Also, women of childbearing age in industrial areas also need special attention to BMI, especially those less than 18.5 kg/m<sup>2</sup>. We recommend that women of childbearing age in these areas have a normal BMI. We need to present this matter because our results show that women of reproductive age with a BMI <18.5 kg/m<sup>2</sup> and having a heterozygous variant SHBG genotype (W/v) is undernutrition. Moreover, it has also been shown that women of childbearing age with a BMI <18.5 kg/m<sup>2</sup> and having the heterozygous variant SHBG genotype (W/v) have lower protein, fat and carbohydrate intake.<sup>32</sup> It has been stated that gene mutations cause abnormalities in protein metabolism in cells. Disorders of protein metabolism in cells cause various forms of organ abnormalities, resulting in congenital abnormalities<sup>33</sup> and morphological variations.<sup>34</sup> Therefore, it is necessary to improve nutrition for reproductive women in agricultural and industrial areas such as in Karawang Regency, West Java Province, Indonesia.

Various natural ingredients can be used as a source of protein. Proteins that are sourced from natural materials can be developed to meet protein intake. Moreover, it has also been shown that proteins from natural ingredients contain several enzymes with the potential for therapy.<sup>35</sup> All the above studies' results that reveal the role of SHBG in both men's and women's reproductive systems clarify the relationship between SHBG and primary infertility. Apart from hormones and SHBG, which can affect primary infertility, it is necessary to discuss pollutants that affect populations in agricultural and industrial areas.

Based on the etiology of infertility in female subjects, this study indicates that PCOS ranks top, which is 26.32% of the total subjects. PCOS is potentially valuable indicators of cultural, environmental, and genetic factors that may contribute to excess risk in certain world regions. It has been proven that the prevalence of PCOS is determined by region and race/ ethnicity.<sup>36</sup> The results of a study in the US showed that the prevalence of PCOS in the southern region was 47.5%, in the central region at 23.0%, while in the western region it was 18.7% and in the northeast region 10.3%.37 Also, it has also been stated that genetic and environmental (lifestyle) factors are associated with the pathophysiology of PCOS after prenatal exposure to androgens.<sup>38</sup> Moreover, environmental toxins, dietary diet, obesity, and geographical variations are associated with PCOS.<sup>39</sup> Besides these pollutants, bisphenol A {2, 2,bis (4-hydroxyphenyl) propane=BPA)} is made by combining acetone and phenol. BPA is used in food packaging and in general as an industrial ingredient. BPA exposure to humans can be through inhalation, skin and digestive tract. BPA has weak estrogenic, anti-androgenic, and antithyroid activity, although it can accumulate in various human body tissues. It has been reported that BPA affects metabolism and the reproductive system in humans. It is more detailed than BPA decreases male and female fertility.40 In more detail, it shows the impact of 2,2-bis 4-hydroxyphenyl propane (BPA) as a water and soil pollutant with PCOS incidence.<sup>41</sup> The results of previous studies showed that the women with PCOS had higher blood levels of BPA than the control group.<sup>42</sup> With the high percentage of primary infertility in this study, research on various pollutants in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia, should be conducted.

Oligoasthenoteratozoospermia in this study reached 33.68% of the population (N=95 subjects). The results of this study are different from study results in India. A study in India showed that 3.8% of 105 men with fertility problems experienced oligoasthenoteratozoospermia.43 We suspect that the high prevalence of oligoasthenoteratozoospermia in the group of infertile men in this study is related to environmental pollutants. It has been explained previously that high pollutant loads are found in the downstream part of the Citarum river, which crosses the Karawang Regency. Our statement follows the research results, which state a significant positive correlation between seminal total PCB level and the percentage of single-stranded DNA in sperm.9

#### **CONCLUSION**

Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate the population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia. Therefore, it requires supervision and protection from the government, society, factory owners, and related health workers. This study is intended to overcome the impact of pollutants that threaten residents who live and work in agricultural and industrial areas in Karawang district, West Java Province, Indonesia. Of course, this is also applied in the other agricultural and industrial areas in Indonesia.

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#### **CONFLICTS OF INTEREST**

The authors declare that they have no competing interests.

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#### **AUTHORS CONTRIBUTIONS**

Conceptualization: AG, RW, DD. Data acquisition: AG, DD, HGW and DK. Data analysis or interpretation: AG, RW, HJE, HGW, DK and DT. Drafting of the manuscript: AG, RW and EP. Critical revision of the manuscript: DD, HJE, HGW and DT. Approval of the final version of the manuscript: all authors.

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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