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Table of Contents
International Islamic Medical Journal
Volume 2 Number 2, June 2021

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Journal Homepage ://journal2.unusa.ac.id/index.php/IIMJ

Clinical Characteristic of Congenital Fetal Anomaly In Tertiary Referral Hospital in East Java, Indonesia

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ABSTRACT

Background: Congenital fetal anomalies were defined as any structural defect present at birth. Congenital fetal anomalies are an important causes of neonatal morbidity and mortality in developed and developing countries that affect health care system. Reliable data on these congenital anomalies are still lacking, especially in Indonesia. Objective: This study aims to determine the characteristic profile of congenital fetal anomaly in single tertiary hospital in East Java, Indonesia. Methods: Retrospective cross-sectional by using medical record data of dr. Soetomo General Hospital on January – December 2017. Results: There were 58 cases (4,3%) with fetal congenital anomaly from 1360 deliveries in 2017. The majority of cases were referral cases (51 cases; 88%) and only seven cases were booked cases in obstetric outpatient dr. Soetomo General Hospital. Most of these congenital fetal anomaly cases (25 cases / 43,1%) were born from mother with ages 20 – 30 years old. Most cases (34 cases; 58,64%) were diagnosed first at third trimester (gestational age > 28 weeks). There were 36 cases (62%) had active termination of pregnancy. Thirty eight percent (22 cases) were born at 37-42 weeks and majority were born section caesaria. The three highest proportion of organ systems involved in fetal congenital anomalies were those of abdomen (22 cases; 37,9%); head (20 cases; 34,5%); thorax and muskuloskeletal (each 12 cases; 20,7%). Conclusion: The incidence of congenital fetal anomaly in dr. Soetomo Hospital at 2017 was 4,3%. Omphalocele and CTEV were two most common types of congenital fetal anomaly found. Most cases of congenital fetal anomalies have a poor prognosis, 67% cases born died. Further research about risk factors and comprehensive database are needed on cases of congenital anomaly to establish appropriate prevention and management.

Introduction

Congenital anomalies are the majority causes of mortality in developed and developing countries. Congenital anomalies are also known as birth defects, congenital disorder or congenital malformation. It can be defined as a structural or functional anomalies that occure during intrauterine life and can be identified prenatally, at birth or later in life (WHO, 2016). Congenital anomalies contribute to perinatal mortality and long-term morbidity that affect on society and health care system. Globally, an estimated 7,9 million children (6 percent of total births worldwide) are born each year with serious birth defect or congenital anomalies[2]. According to the World Health Statistics 2012, about 7% of all under-five

deaths globally are caused by congenital anomalies (WHO, 2012). Congenital malformations contribute to: 1.4% of deaths in the age group 0–6 days of life; and to 19% of deaths in the age group 7–28 days (Ministry of Health, Republic of Indonesia, 2010). Among infants with malformation who do not survive, more than 70% die in the first month of life. Approximately 40% to 60% are unknown origin. The etiology of congenital malformation is genetic (30-40%) and environmental (5 to 10%). Among the genetic etiology : chromosomal abnormality constitutes 6%, single gene disorders 25% and multifactorial 20- 30% (Rajangnam *et al*., 2007).

Dr. Soetomo General hospital is the only tertiary referral hospital center in eastern Indonesia, and handles many referal cases of congenital anomaly. This study aims to determine determine the pattern and characteristic profile of congenital fetal anomalies in single tertiary referral hospital in East Java, Indonesia.

Methods

This study was a cross-sectional retrospective study using electronic medical data records in dr. Soetomo General Hospital at January 2017 until December 2017. The inclusion criteria of this study were cases with congenital fetal anomaly that have been performed ultrasound examination and born in dr. Soetomo General Hospital. Exclusion criteria were infants which born outside dr. Soetomo General Hospital. The data obtained were collected about clinical information including: maternal profile (maternal age, parity, previous birth history abnormality), gestational age when first diagnosed, gestational age at termination, mode of delivery, amniotic fluid volume and prognosis of fetus. The diagnose of congenital fetal anomaly was made by routine ultrasound during pregnancy follow up and by referred hospital which was then reconfirmed in dr. Soetomo General Hospital. From these data, we traced the type of congenital anomaly was found, infant's outcome and appropriateness of abnormalities obtained during ultrasound with at birth.

Results and Discussion

A total of 58 cases (4,3%) with fetal congenital anomaly of 1360 births at Dr. Soetomo General Hospital were recorded during January 2017 until December 2017. We found 2 cases with conjoint twin. The majority of cases were referral cases (51 cases; 88%) and only seven cases were booked cases in obstetric outpatient dr. Soetomo General Hospital. Maternal profile of congenital fetal anomaly in dr. Soetomo Hospital at 2017 based on maternal age, maternal parity and previous birth history can be seen in Figure 1.

Nineteen cases (32,8%) were born to mother aged over 35 years, fourteen cases (24,1%) born to mother aged 30-35 years, twenty five (43,1%) born to mother aged 20-30 years. Many studies proves that increased maternal age is a risk factor for congenital abnormalities. It was caused by the correlation between advanced maternal age with chromosomal abnormality in fetus. A three-years prospective study from India showed that maternal age has statistically significant association with congenital fetal anomalies (Thaddanee *et al*., 2016). However, this was contrary with our study. It may be due to small number of cases included in this study and only one year study.

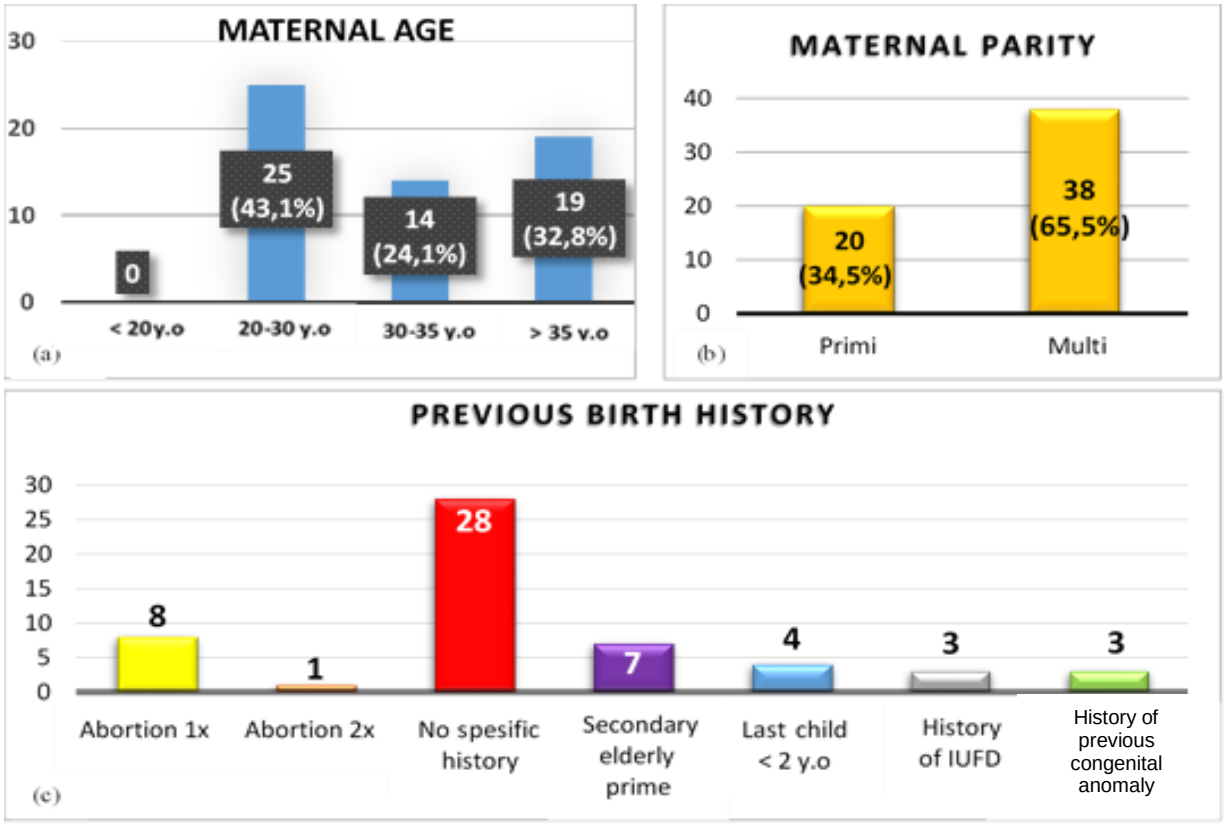

Figure 1. Maternal profile of Congenital Fetal Anomaly in dr. Soetomo Hospital at 2017 based on (a) Maternal Age, (b) Maternal Parity, (c) Previous Birth History

Based on maternal parity, thirty eight cases (65,5%) were multipara and twenty cases (34,5%) were primipara. This is consistent with research conducted in India at 2013 that congenital fetal anomalies were more frequent in multipara compared to primipara (Sarkar, *et al.*, 2013). The other study by Patel also showed that incidence of congenital malformation was higher in multipara (Patel and Chaudary, 2017). Based on multiparous cases in this study, there was several previous birth history abnormality such as abortion (9 cases), the pregnancy distance from last child $\geq$ 10 years or secondary old prime (7 cases), last child less than 2 years old (4 cases), history of intrauterine fetal death (IUFD) in previous pregnancy (3 cases), history of congenital abnormality in previous pregnancy (3 cases). There were twenty eight cases which no specific history in previous birth. The characteristic of pregnancy profile in congenital fetal anomaly's cases at dr. Soetomo Hospital can be seen in table 1 below.

Most of them (34 cases; 58,64%) were diagnosed at gestational age in third trimester (> 28 weeks). Twenty three cases (39,66%) were diagnosed at second trimester (gestational age 15-28 weeks) and only one case was diagnosed at first trimester (gestational age 0-14 weeks). This was happened because many referral cases came to dr. Soetomo Hospital at the second and third trimester. Thirty eight percent (22 cases) were born in aterm (gestational age 37-42 weeks) and the others (36 cases; 62 %) were born in preterm (gestational aget less than 37 weeks) . This study is inconsistent with other researches in India that showed most cases of malformed babies were born aterm (Patel and Chaudary, 2017; Dutta *et al.*, 2010).

Table 1. Characteristic of Pregnancy Profile in Congenital Fetal Anomaly's Cases at dr. Soetomo Hospital

Pregnancy profile		n (%)
Gestational age at first diagnosed	0-14weeks	1 (1,7%)
	15-28 weeks	23 (39,66%)
	>28 weeks	34 (58,64%)
Gestational age at labor	<20 weeks	2 (3,5%)
	20-28 weeks	2 (3,5%)
	28-34 weeks	15 (26%)
	34-37 weeks	17 (29%)
	37-42 weeks	22 (38%)
Prognosis	Dubia ad bonam	1 (2%)
	Dubia ad malam	34 (58%)
	Dubia	23 (40%)

The study in Dr. Wahidin Sudirohusodo Tertiary Hospital, Makassar, Indonesia at 2016 showed that 68% babies with congenital fetal anomaly were born at gestational age ≥ 37 weeks (Lestari and Febriani, 2017). It possibly happened because in this study, there were more cases of congenital fetal anomaly that had poor prognosis (34 cases; 58%) so that active pregnancy terminations were carried out before term. It was only one case of congenital fetal anomaly with prognosis of dubia ad bonam, others (23 cases; 40%) still had uncertain prognosis (dubia).

In this study, we also evaluate the characteristic of pregnancy termination in congenital fetal anomaly's cases based on: active and spontaneous termination, the reason for active termination of pregnancy and mode of delivery. It summarized in figure 3.

Of 58 congenital fetal anomaly's cases, there were 36 cases (62%) had active termination of pregnancy, others (22 cases; 38%) had a spontaneous labor. The reason of active termination of pregnancy can be seen in figure 3 (b). Sixteen cases (44,4%) were terminated due to term gestational age, eight cases (22,2%) due to IUFD (intra uterine fetal death), five cases (13,9%) due to family decision of bad prognosis, others due to severe oligohidramnion, severe preeclampsia and mirror syndrome. Mode of delivery of congenital fetal anomaly's cases can be seen in figure 3 (c). Most cases

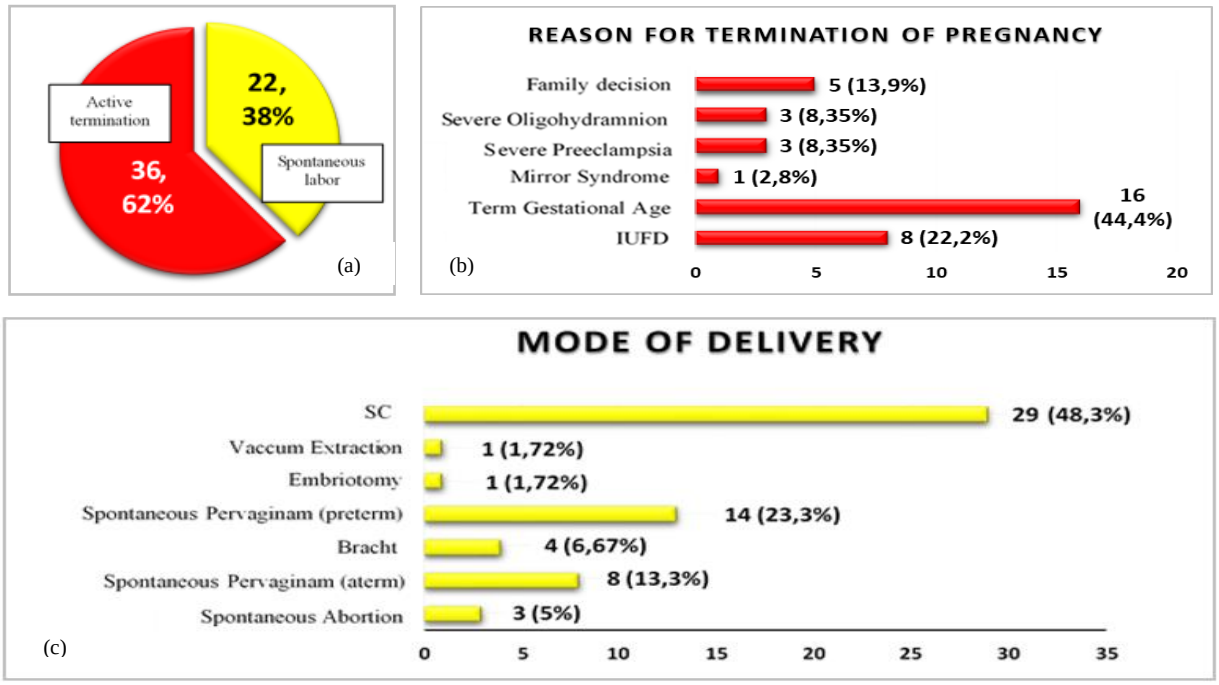

Figure 3. Characteristic of Pregnancy Termination in Congenital Fetal Anomaly's Cases based on: (a) active and spontaneous termination, (b) reason for active termination of pregnancy, (c) mode of delivery

(29 cases; 48,3%) were born sectio caesarian. The study by Wills also shows that most cases of congenital anomalies were born caesarian (59,1%) and mainly done for obstetric indication (Wills, *et al.*, 2017).

Table 2 shows the description about organ systems that involved in 58 cases of congenital fetal anomaly. This study found 19 cases (33%) were born with single type of congenital fetal anomaly and others with multiple anomalies (39 cases; 67%).

Table 2. Description about Type of Congenital Fetal Anomalies according to Organ Systems that Involved in dr. Soetomo General Hospital

Organ Systems (%)	**Type of congenital fetal malformation**		**n**
Head (34,5%)	Facial	Ear Malformation	1
		Cleft Lip Palate	3
		Microcephaly	1
		Dolichocephaly	1
	Central nervous systems	Anencephaly	1
		Dandy Walker Syndrome	2
		Hydrocephalus	3
		Holoprosencephaly	3
		Meningoencephalocele	3
		Meningocele	2
Thorax (20,7%)	Non Cardiovascular	Congenital Hydrothorax	1
		Lung Hypoplasia	2
	Cardiovascular	Truncus Arteriosus	1
		Ectopia Cordis	1
		Dilated Cardiomyopathy	2
		VSD	2
		PDA	1
		Eibstein Anomaly	1
		Multiple Heart Anomalies	1
Musculoskeletal (20,7%)	Extremities	Micromyelia	1
		Syndactyly	1
		Polydactyly	3
		CTEV	7
Abdomen (37,9%)	Gastrointestinal Tract	Diaphragmatic Hernia	1
		Duodenal Atresia	2
		Omphalocele	13
		Congenital Megacolon	1
		Gastroschisis	3
	Urinary Tract	Hydronephrosis	2
Hidrops foetalis (15,5%)			9
Body Stalk Anomaly (3,4%)			2
Conjoint twin (3,4%)			2
Acardiac twin (1,7%)			1

The three highest proportion of organ systems involved in fetal congenital anomalies were those of abdomen (22 cases; 37,9%); head (20 cases; 34,5%); followed by thorax and muskuloskeletal (each 12 cases; 20,7%). The study in India conducted by Patel in 9600 malformed babies showed that the three most common system involved were cardiovascular system (23,4%), musculoskeletal system (23,4%) and gastrointestinal tract (15,9%) (Patel and Chaudary, 2017). The results of surveillance of the Ministry of Health of the Republic of Indonesia with 28 selected

hospitals in 18 provinces from September 2014 to March 2018 showed that 1085 infants with birth defects were reported. It showed that the most common congenital abnormalities were involved 21,9% the musculoskeletal system (talipes equino-varus); 20,4% orofacial cleft; 18,4% the nervous system (neural tube defect); and 16,14% abdominal wall defect (Ministry of Health, Republic Of Indonesia, 2018). The study from Mustofa *et al.,* in four teaching hospital in Indonesia showed the most of congenital anomalies involved gastrointes-tinal tract (25,8%) Mustofa *et al.*, 2009). The data about the most common type of congenital anomalies in Indonesia varies depending on each region. The differences of the most common type of congenital fetal anomalies between studies might be related with different race, ethnic, geographic and social factors.

There were two cases with conjoint twins so the total infant with congenital fetal anomaly were 60. We described about fetal's gender, fetal birth weight, APGAR scoret and we traced the infant's outcome. It can be seen in table 3.

Table 3. Infant's Outcome of Congenital Fetal Anomalies's Cases in dr. Soetomo Hospital at January – December 2017

Infant Outcome		**n (%)**
Infant's Gender	Female	31 (51,7%)
	Male	23 (38,3%)
	Ambiguous	6 (10%)
Fetal Birth Weight (grams)	< 1000	10 (16,7%)
	1000-1500	5 (8,3%)
	1500-2500	25 (41,7%)
	≥2500	20 (33,3%)
APGAR Score	0	13 (22%)
	1-3	29 (48%)
	4-6	11 (18%)
	7-9	7 (12%)
Infant's Outcome	Died	40 (67%)
	Live	20 (33%)

Thirty one infants (50%) were female, 23 infants (37%) were male and 8 infants (13%) can not be differentiated (ambiguous). There were 40 cases (67%) of congenital fetal anomaly died. The limitation of this study is we did not evaluate and follow the infant's growth and development after birth.

We tried to evaluate the congruence between fetal abnormalities found during ultrasound and abnormalities at birth. Fifty five cases (94,8%) of congenital fetal anomaly obtained to be appropiate between ultrasound result and anomaly found at birth. There were two cases with undetected anomalies in ultrasound. One case could not be identified due to the infant born stillbirth and did not perform post mortem autopsy.

Conclusion

The incidence of congenital fetal anomaly in dr. Soetomo Hospital at 2017 was 4,3%. The majority of congenital fetal anomaly's cases had multiple anomalies (39 cases; 67%). Omphalocele and CTEV were two most common types of congenital fetal anomaly found. Most cases of congenital fetal anomalies have a poor prognosis, 67% cases born died. There were 94,8% compatibility between ultrasound results and abnormalities found at birth in cases of congenital fetal anomaly at dr. Soetomo Hospital. Further research is needed to determine the risk factors in cases of congenital fetal anomaly at dr. Soetomo General Hospital.

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Exploring Past, Present and Future of Orthotics and Prosthetics in Pakistan

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ABSTRACT

This is a qualitative study to explore the perception of Orthotists and Prosthetists regarding past, present and future of their profession. The Qualitative research approach using individual interviews. Data was collected from professionals of some private and some government sector in Rawalpindi, Peshawar and Lahore during April 2019 to July 2019. The sample size was 12. A demographic questionnaire and standarized instrument from Nvivo was filled satisfying the inclusion criteria. A comprehensive audio-videography have been developed, recorded, transcripted and documented. Data was transcribed and thematic analysis along with characteristics was drawn manually. Data verification was done with the help of coders. After the extraction of data followings results are emerged. General category themes are trainings and seminars, opportunities, government setup, lack of coherence among professionals, uniform curriculum, and establishment of council, effects of earthquake, German contribution and techniques/technology. Barriers are identified at the level are lack of awareness/ acknowledgement, low job opportunities, no proper workshops, poor referral system, limited resources and old technologies. It is concluded that the field of orthotics and prosthetics in Pakistan need attention in the following categories i.e. trainings and seminars, job opportunities, uniform curriculum, unity among professionals, establishment of council, acknowledgment at government level and awareness among other health professionals.

Introductions

The prosthetic and orthotics profession prosthetics and orthotics profession is involved in the manufacture and facility of orthopedic appliances for amputees (potential prosthetic users) and persons with other physical incapacities. The preponderance of developing countries has no regular prosthetic and orthotic (P&O) training. This happens in the inadequate availability of prosthetic and orthotic aids for people with physical disadvantages. It is expected that in 2010, 30 million people in Africa, Latin America, and Asia, need assistive tools about 0.5% of the population in the emerging society (Magnuson and Ramstrand, 2009). The majority of these people could be re-established within the community they took an assistive tool to facilitate mobilization, known as a first level to retrieve fundamental rights, food, education, and income (Thomas and Thomas, 2003). The fields of otrhotics and

prosthetics have always served great human necessities and have been on constant iterest to the scientists and discoverers for centuries (Khasnabis, *et al.*, 2010).

Cold war conflicts during world history have occurred in remarkable mortality and morbidity, including grotesque wounds and the loss of limbs. These countless battle victims have provided the impetus for the development of substitute limb design. After World War II, the innovation of prosthetic device design become even further, after that the National Academy of Sciences founded the Artificial Limb Program (Awais et al., 2012).

Based on report rates, The First World War created so many disabled bodies. In April 1915, 3000 disabled veterans had returned to Great Britain, only four months into its war. At final calculation, Britain had some 752,000 newly disabled people; Germany admitted 4 million injured and 1,537,000 with permanent disabilities, and France had more than 1 million newly disabled. Canada, fielding an approximately small unit in contrast to other belligerents, had some 70,000 disabled veterans, while the United States, even with entering the war late in 1917, estimated for approximately 200,000 (Gerber, 2012).

The causes for the loss in medical recovery help are not intuitive. Except it is suspected that a person with a disability will die as an outcome of the disability, the cost-effectiveness of recovery to the disabled self, to their family, and their society seems evident. Even the disadvantaged nations have a sufficient population of the middle class or well-off persons to both need and help medical recovery. Yet it is mostly missing (Healy et al., 2018).

The absence of a path to health and recovery help, knowledge and vocation, and the high price of medical charges, restrict the capacity of people with disabilities to fully interact in their societies. Injury restriction will reduce the reasons for disabilities and developed care and help will better the lives of people being with injury-related disabilities (HHRD, 2012).

To understand the causes why medical rehabilitation has not become a part of various healthcare systems, it is essential to look at historic, ethnic, political, and financial factors. Unluckily very few studies have been assumed in developing nations, where mobility and physical capabilities are so vital.

By the end of the year 2004, about 600 million people in the world had several types of disabilities and this number is increasing because of ageing, chronic diseases, conflicts and wars and road traffic mishaps etc. The increased rate of the disabled population is requiring great demands for rehabilitation services. Just about 80% of the disabled population belongs to developing countries; including Pakistan (Mills et al., 2021).

Prosthetics-orthotics offer better than common occupational stability, as there are thousands of amputees and paralytics in the necessity of substitute limbs and supports. No acceptable means for manufacturing prostheses and orthosis in many measurements, like shoes, has been developed. Custom lilting may be improved and made more efficient, as is being created now through research, but the replacement of the basis for such lilting does not seem to be forthcoming. The discovery of means for resettling nerves to revitalize paralyzed limbs, or of serum for stimulating the amputee's body to grow new limbs would surely change prosthetics-orthotics as we know it now, and it would be ill-considered to say that such developments are difficult in light of some of the current research in

the configuration and role of the cell. However, prosthetics-orthotics is seemingly no more subject to outmodedness than most expert fields, and perhaps few so than many (WHO, 2010).

Then socio-demographic and epidemiological evolution in growing countries has remodeled the morbidity and death pattern among populations. This has brought non-transmittable diseases to the forefront of the healthcare delivery policy. Within this group, a disorder correlated to the nervous system constitutes a substantial proportion inducing morbidity, mortality, disability, and quality of living (Pakistan Federal Bureau of Statistic, 2010).

According to the information of World Health Organization on the occurrence of disability, about one million people in Pakistan require prosthetic or orthotic rehab services. The bigger part of such population is unable in accessing P&O services and as a result prohibiting their inclusion into the society. Allotting resources to the rehabilitation of these disabled people can make them important providers to the society. Irrespective of the incremental progressions made in the last 2 ½ decades, the bulk of the disabled population in Pakistan does not have an approach to even basic rehab services and also they are deprived of their elementary human rights (Awais et al., 2012)

Disability is a shame in Pakistan, and cultural traditions are an interruption to the integration of the disabled into society. Further limitations to addressing the necessities of the disabled include the loss of unfailing disability epidemiologic data, lacking funding and inadequate health care system, and workforce shortages (Magusson, 2009).

The requirement for a high-quality prosthetics and orthotic education program in Pakistan is heightened by the event of disability in the country. In Pakistan, the recorded frequency of locomotors' disabilities ranges from 0.3%-0.83% (HHRD, 2012). Pakistan's repeated fight with terrorism issued a subsequent growth in the incidence of amputation. Furthermore, Pakistan is one of four nations in the world that are still polio-endemic. The majority of patients infected with polio need orthosis (Statistic Government of Pakistan, 1998). The earthquake in October 2005 produced 750 amputees at altered levels and 650 paraplegic patients within Northwest Frontier Province and the Kashmir district (Awais et al., 2012).

Pakistan's health pointers, health infrastructure and level of funding are generally underprivileged, especially in rural areas. There is no government-sponsored health insurance organization, but private health insurance is obtainable for those few who can afford it. A government employee becoming disabled during the course of work is usually allowed to a disability grant and medical benefit. Most of the population, therefore, does not have access to suitable health care (Sidra, *et al.*, 2011).

Methods

This study was initiated after approval from advanced study & research committee (ASRC) of Isra institute of rehabilitation sciences, Isra University Islamabad. A total of 12 professionals, inclusion and exclusion criteria were recruited in the study. Researchers/ Clinicians were asked to give individual interviews one to one. In the interviews, questions were asked from a self-structured questionnaire. The informed consent was taken prior to collection of data. The data was analyzed through N Vivo software.

S#	Theme	Characteristics
1	Trainings and Seminars	Professional enhancements, development of knowledge regarding advancements in the field, Exposure to different approaches, Organization should bear the cost, trainers are not available so foreigner trainers should be needed
2	Opportunities	Jobs opportunities are rare and really difficult to find a good opportunity. No suitable salaries
3	Government Setup	Few government setups with lack of advanced workshops. No acknowledgement. Low awareness in the public sector
4	Lack of Coherence among professionals	No unity, no common platform, very slow advancements. Because of this more quacks being benefited
5	Uniform curriculum	Lack of uniform curriculum which leads to groups of P n O's with different school of thought. No accurate balance among theory and practical skills learning
6	Establishment of Council	For the steady growth and improvement in the field, establishment of council is very compulsory which is still in process. Due to its absence the development was very slow almost stagnant
7	Effects of Earthquake	Many institutes initiated this course after the Earthquake in 2005. A lot of patients were treated and more trained P n O's were required.
8	Germans Contribution	Foreigners especially Germans played really important role in the establishment of this field in Pakistan as they came to treat Afghan war refugees and trained the locals the basic skills.
9	Techniques/ technology	ICRC Polypropylene technology is mainly used for prosthesis.

Results

	Barriers
1	There are no job opportunities in the government sector.
2	In private sector there is no fixed salary so P n O's are being exploited
3	There is lack of government set ups.
4	No awareness or acknowledgement in the government sector
5	P n O's are not being acknowledged like other health professional i.e. physiotherapists
6	Lack of proper workshops
7	There is no unity among the professionals
8	Absence of council leads to many different school of thoughts which create problems for P n O's to work together
9	No proper referral system
10	Very old techniques and technologies are used in this field. Because of low budget and limited resources.
11	Low awareness among the other health professionals
12	Evolution of this field is slow almost stagnant because of advancements and improvements in the education system
13	Most of the teachers who are teaching BS (hons) P n O, are only bachelor's degree. Only one university is offering Master's degree
14	There are no known NGO's who financial support the treat of this field and health insurance doesn't include prosthetics treatment.
15	Very limited resources. Low funding's
16	There is lack of uniform curriculum. Present curriculum is not according to the international standards.
17	There is unequal distribution of syllabus between practical skills and theory.
18	There is no check and balance from any authority
19	Lack of quality education
20	Faculty in most of the institutes is not qualified up to the international level

Discussion

The importance of trainings and seminars cannot be denied. Trainings should be conducted on the regular intervals by different organizations and not only one or two organization can be responsible for conducting the trainings. Every institute should conduct the trainings for their workers and should send them for the trainings on regular basis. It will be really helpful for the growth and development of the institute as it will help their workers to get the exposure of different approaches being used in the field of orthotics and prosthetics not only in Pakistan but all over the world. It is the responsibility of the institute to bear the expenditure for the trainings and seminars. In the long run the expenditure will serve them back.

Job opportunities in the field of orthotics and prosthetics are really low. Unemployment can cause depression in the young lot of the society which can be harmful on the national level. This field couldn't get the acknowledgement until and unless if every government set up has orthotics and prosthetics department with orthopedic department. There should be separate OPD's where P n O's can examine the patients.

The main reason due to which this field is not flourishing the way it should be is the lack of coherence among the professionals. The pioneers and experienced people of this field see each other as the competitor rather than a coworker. This is due to lesser interactions among them. If they are in contact with professionals of their own field then they can get the useful ideas by discussing with each other. Because of no unity among the professionals many quacks are getting benefited.

The following quote is taken from the post conference document of the ISPO Conference held in Dortmund, Germany, 2004. "It was obvious early in the conference and from the survey returns that a countless deal of resemblances exist between prosthetic and orthotic practitioners both in terms of professional capabilities and educational needs. These resemblances directed that these professionals work in a recognized and distinct way in supplying prosthetic and orthotic care to patients in many countries in Europe and thus should be recognized as one professional group, known as Prosthetists and Orthotists. Although a number of variances in models and trails of education existed between the countries represented, ambassadors agreed upon the need for a common set of standards of education and learning objectives for student Prosthetists and Orthotists in Europe. This was perceived as important in confirming appropriate care for persons using prosthetic and orthotic devices (Magnusson et al., 2016).

For the betterment of this field in Pakistan we need to establish a council of orthotics and prosthetics like any other discipline of medical field. Under the council P n O's can work together for the development of the field. There is no proper platform which can work for the development and betterment of the field. The establishment of council can provide a place to P n O's where they can ask for help in any kind of difficulties.

The earthquake of 2005 was a turning point in the establishment of orthotics and prosthetics in Pakistan. Before the earthquake there were not enough employment opportunities and awareness for all the qualified P&Os and the field.

The October 2005 earthquake was the most damaging natural disaster in the

country's past in terms of the number of people killed or injured. There were numerous survivors with extreme disabilities, such as spinal cord injury, traumatic brain injury, amputation, and long bone fractures. Their management and recovery involved rehabilitation doctors, mainly from the armed forces (Rom & Kelman, 2020).

Germans played a very vital role in the history of orthotics and prosthetics in Pakistan. They initiated this field in Pakistan. They started treating the refugees of the Afghan war. They trained the locals to be skillful to deal the patients when they are gone. In the beginning the PIPOS started this course and they hired teachers mainly from Germans who had graduation degree in the relevant field

The main problem we face in practical aspect of this field is not the technical skills but the advancements in technology. The lack of updated knowledge abstain us from developing new methods which can preserve not only P n O's energy but also benefit the patients both financially and physically. We should not only focus on enhancing the technical skills but also advanced technology. By every passing day there is a new discovering in the field of orthotics and prosthetics, but unfortunately most of the P n O's are still using the techniques which were being taught in the beginning of this field.

Conclusion

D From the perspective of participants it was concluded that the up gradation and upkeep of this field is very necessary for the betterment and development.

Mostly participants had issues regarding the job opportunities they think that it is necessary for every government hospital to have orthotics and prosthetics department. Government needs to understand the importance of this field in the rehabilitation. There are not enough jobs for the fresh graduates, so this field is getting saturated with unemployed P n O's.

There are no proper trainings arranged by the institutes to enhance the abilities of P n O's. Old technology and old techniques are still in use even in much known rehabilitation institutes.

Another factor which was concluded by this research was that the participants were not satisfied by the unity of the professional in their field. They felt an immense need of a platform where they can get together to understand the problems of other P n O's. If they could get a proper platform where they can get their rights then will try to come united. Unity is the basic problem which is being faced in our field. We need to understand that sharing the knowledge and making collaboration is very necessary for the development of this.

It was further concluded by interviews of the participants that there is no uniform curriculum which is the basic need to provide good education and give a good base to the P n O's. By setting a uniform curriculum we can solve many problems.

Recommendations

Every government hospital has the department of Orthotics and prosthetics. Government setups should provide jobs to the fresh graduates. By making new set up on the government level will definitely overcome the problem job opportunities and it will also lesser the load of the patients.

Proper trainings and seminars should be arranged to overcome the lacking of up to date knowledge. Trainings can be arranged

in the country by appointing foreigner trainer to conduct it for our P n O's in such a way we can train more P n O's . Every institute should take this initiative to send their P n O's to the developed countries for the trainings and exposure to the advanced knowledge. There should be a uniform curriculum according to ISPO professional profile. Establishment of council is really compulsory for the betterment of field. Orthotics and prosthetics schools should implement a professional advisory system. They should have a member of the disabled community on advisory

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The Effects of Turmeric Infusion and Turmeric Juice (Curcuma Domestica) on The Staphylococcus Aureus Growth in Vitro

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ABSTRACT

Background: Turmeric is a plant that grows in tropical areas and functions as medicine. The chemical compounds contained in turmeric have a role as antioxidants, antimicrobials, anti-cancer, indigestion, smallpox, insect bites. The *curcumin* content in turmeric has antibacterial activity against various types of Gram negative, Gram positive, antiviral and anti-tumor bacteria. Essential oils can be used as antibacterial because they contain hydroxyl and carbonyl functional groups which are phenol derivatives. Flavonoids can interfere with cell wall formation with peptidoglycan *transpeptidase* activity which will break down cell walls and damage cell membranes so that important components such as proteins, nucleic acids, nucleotides will be lysis. Staphylococcus bacteria are normal flora on the skin, respiratory tract, and digestive tract of food in humans. These bacteria can cause disease when they reach 1,000,000 or 106 per gram, an amount sufficient to produce the toxin. S. aureus bacteria can cause various types of infections ranging from minor skin infections, food poisoning to systemic infections. The aim of our study was to analyze the effects of infusion and turmeric juice (Curcuma domestica val) on the growth of bacteria Staphylococcus aureus through invitro. Method: This study is a laboratory experimental study with the aim of analyzing turmeric infusion (Curcuma domestica val) and turmeric juice effect on the growth of staphylococcus aureus by invitro. This research was conducted in an integrated laboratory, FK UNUSA. The samples in this study were 4 replications per treatment. The independent variables in this study were turmeric infusion and turmeric juice (with a concentration of 10%, 30%, 50% while the dependent variable in this study was the growth of Staphylococcus aureus bacteria. Data analysis used was the one way ANOVA test and Pearson correlation to determine the effect of giving turmeric infusion and turmeric juice on the growth of bacteria staphylococcus aureus through invitro. Result: The average growth of bacteria in the turmeric infusion in group I (control), 10%, 30% and 50% of turmeric infusion was 4.89 ± 0.4425 log CFU / ml, 3.07 ± 0.61330 log CFU / ml, 2.99 ± 0.63986 log CFU. / ml and 3.02 ± 0.22650 log CFU / ml. The average growth of this bacteria in giving turmeric juice in group I (control), giving 10%, 30% and 50% turmeric infusion was 4.89 ± 0.04425 log CFU / ml, 4.40 ± 0.18355log CFU / ml, 3.10 ± 0.58926 log CFU / ml and 3.02 ± 0.38206 log CFU / ml. Conclusion: In this study, found that there was an effect of giving turmeric infusion and turmeric juice (Curcuma domestica val) on Staphylococcus aureus growth and there was an effect of giving multilevel doses of turmeric infusion and turmeric juice (Curcuma domestica val) on Staphylococcus aureus growth through invitro.

Introduction

Turmeric is a plant that grows in tropical areas and functions as medicine (Hartati & Balittro, 2013). The chemical content contained in turmeric is essential oil, fatty oil, curcuminoid compounds, alkaloids, tannins, flavonoids, glycosides and carbohydrates (Gupta et al., 2015). The

chemical compounds contained have a role as antioxidants, antimicrobials, anti-cancer, indigestion, smallpox, insect bites (Hartati & Balittro, 2013). Curcumin in turmeric has antibacterial activity against Gram negative, Gram positive, antiviral and antitumor (Bernawie, 2006). Flavonoids can interfere with the formation of cell walls with peptidoglycan transpeptidase activity which will break down cell walls and damage cell membranes so that important components such as proteins, nucleic acids, nucleotides will lysis (Dewi, 2015).

Staphylococcus bacteria are normal flora on the skin, respiratory tract, and digestive tract of food in humans. These bacteria are also found in the air and the environment (Warsa, 1994). These bacteria can cause disease if it has reached the amount of 1,000,000 or 106 per gram, an amount sufficient to produce toxins (Taylor, 2020). S. aureus infection is the common bacterial infections and is the causative agent for a variety of human infections, including infective endocarditis, bacteremia, skin and soft tissue infections, osteomyelitis, septic arthritis, prosthetic device infections, lung infections, gastroenteritis, meningitis, toxic shock syndrome, and urinary tract infections (CDC, 2019).

The purpose of this study was to analyze the effect of infusion and turmeric juice (Curcuma domestica val) on the growth of Staphylococcus aureus by invitro.

Methods

This research is a laboratory experimental research. The research materials used were turmeric infusion and turmeric juice made from turmeric obtained from turmeric farmers in Pengampon, Setro – Menganti, Gresik. The bacterium used was Staphylococcus aureus obtained from BBLK Surabaya. The media used were nutrient broth and MSA (Manitol Salt Agar).

Making Turmeric Infusion

The preparation of turmeric infusion is by peeling the turmeric, then washing the turmeric using distilled water then grating the turmeric using a grated then adding 100 mL of distilled water to make a concentration of 10%, 30% and 50% treatment then heated to a boil for 15 minutes. After that, the infusion is filtered to separate the simplicia using filter paper.

Test The Effect Of Turmeric Infusion On Staphylococcus Aureus Growth

Each 1 ml of Staphylococcus aureus suspense in a nutrient broth with a density of 1.5 x 106 CFU / ml was put into a test tube that had been given 1 ml of turmeric infusion with a concentration of 10%, 30% and 50% then incubated 24 hours at 37o C. After incubation, each mixture was diluted ten times using H2O, then 0.1 ml of each dilution was planted in (Mannitol Salt Agar (MSA) and then incubated for 24 hours at 37ºC, and count the Staphylococcus aureus colonies.

The Test of effect of giving turmeric juice on the growth of Staphylococcus aureus

Each 1 ml of Staphylococcus aureus suspense in a nutrient broth with a density of 1.5 x 106 CFU / ml was put into a test tube that had been given 1 ml of turmeric juice with a concentration of 10%, 30% and 50%, then incubated 24 hours in a temperature 37º C.

After incubation, each mixture was diluted ten times using H2O, then 0.1 ml of each dilution was planted in Mannitol Salt Agar (MSA) and incubated for 24 hours at 37ºC, then count the Staphylococcus aureus

colonies. Number of replications for each group in this study was 4. The study was conducted at the Laboratorium Terpadu FK UNUSA Surabaya in September 2019-March 2020.

Sampling was done using consecutive sampling technique. Inclusion criteria: Staphylococcus aureus bacteria ATCC 25923, Exclusion criteria: Bacteria that do not grow on MSA media.

The variables studied in this study were Staphylococcus aureus groowth with the treatment of turmeric infusion and turmeric juice (Curcuma domestica val) with a concentration of 10%, 30%, 50%.

All data were tested for normality with the Kolmogorov-Smirnov. If a normal value is obtained, the data analysis technique used to prove the first and second hypotheses is one-way ANOVA with an error rate of 5%. If there is a significant difference, then to determine the difference between treatments, the LSD (Least Significant Difference) test or the Least Significant Difference Test is used. The data analysis technique used to prove the third and fourth hypotheses is Pearson correlation.

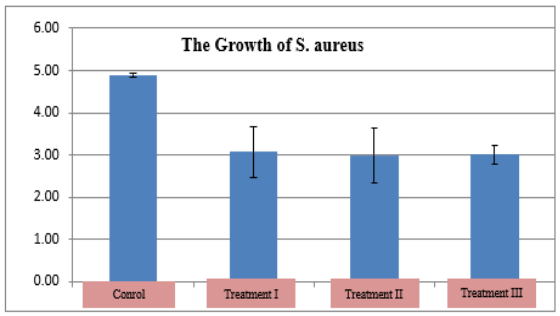
Result

Growth of Staphylococcus aureus with the addition of turmeric infusion

Table 4.1 Staphylococcus aureus growth in log CFU / ml on 10%, 30% and 50% turmeric infusion.

Group	Number of replications	Mean ±SD colony
Control	4	4.89 ± 0.4425
Treatment I (infusion 10%)	4	3.07 ±0.61330
Treatment II(infusion 30%)	4	2.99 ± 0.63986
TreatmentIII(infusion 50%)	4	3.02 ± 0.22650

From table 4.1, it can be seen that the average growth of bacteria occurred mostly



in group I (control), namely 4.89 log CFU/ml with standard deviation of 0.4425 and the least in treatment group II (30% level), namely 2.99 log CFU / ml with standard deviation of 0.63986.

Figure 4.1 Staphylococcus aureus growth in log CFU / ml on 10%, 30% and 50% turmeric infusion

Based on Figure 4.1, it can be seen that the growth rate of Stafphylococcus aureus bacteria was mostly in the control group, while in the treatment groups I, II and III the number of growth tended to be the same.

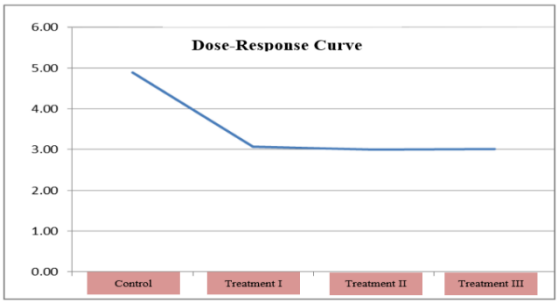


Figure 4.2 dose-response curve of staphylococcus aureus growth with the addition of turmeric infusion

Based on Figure 4.2, the response to the growth of staphylococcus aureus by giving turmeric infusion with levels of 10%, 30% and 50% decreased compared to controls with almost the same number of bacterial colony growths.

Growth of Staphylococcus aureus with the addition of turmeric juice

Table 4.2 Staphylococcus aureus growth in log CFU / ml on 10%, 30% and 50% turmeric juice.

Group	Number of replications	Mean ± SD Colony
Control	4	4.89 ± 0.04425

Treatment I (infusion10%)	4	4.40 ± 0.18355
Treatment II (infusion30%)	4	3.10 ± 0.58926
Treatment III (infusion 50%)	4	3.02 ± 0.38206

From table 4.2, it can be seen that the average growth of bacteria occurred most frequently in the control group, namely 4.89 log CFU / ml with standard deviation of 0.4425 and the least in the treatment group III which was 3.02 log CFU / ml with standard deviation of 0.38206.

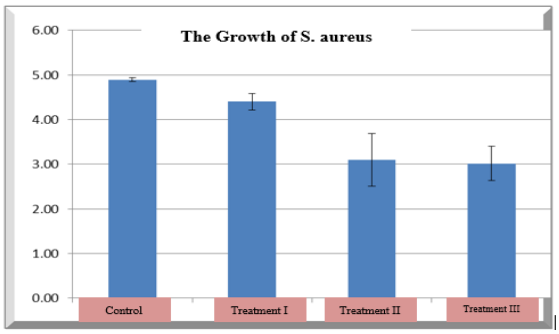


Figure 4.3 Staphylococcus aureus growth in log CFU / ml on turmeric juice with levels of 0%, 10%, 30% and 50%

Based on Figure 4.3, it can be seen that the number of Staphylococcus aureus bacteria growth was mostly in the control group, while the treatment groups II and III tended to be the same.

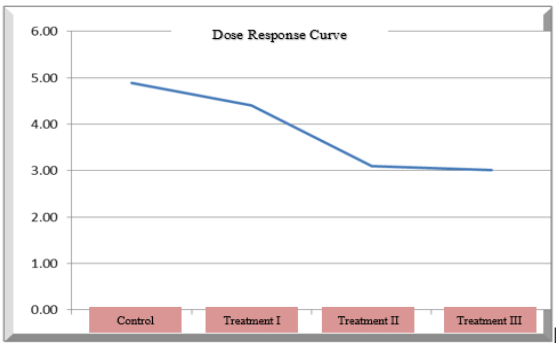


Figure 4.4 Growth dose-response curve of Staphylococcus aureus with the addition of turmeric juice

Based on Figure 4.4, the response on the growth of staphylococcus aureus through giving turmeric juice tended to decrease at the addition levels; but only slightly decreased in treatment II and III.

Treatment group	Significance
Giving turmeric infusion	.189c
Giving turmeric infusion	.200c,d

Data Analysis

Data Normality test

Table 4.3 Staphylococcus aureus growth normality test by giving turmeric juice infusion

Based on the normality test, the p value of the tested bacteria was given by giving turmeric infusion of 0.189 and giving turmeric juice of 0.200. Both of these p values are greater than 0.05, so it can be concluded that the growth data of staphylococcus with infusion or turmeric juice is normally distributed.

Table 4.4 One Way Anova test on the effect of infusion and turmeric juice on the staphylococcus aureus growt.

Treatment group	Significance
Giving turmeric infusion	.000
Giving turmeric infusion	.000

Based on table 4.4 above, the significance value of the One Way Anova test giving infusion and turmeric juice on the growth of Staphylococcus aureus is 0.000 and 0.000, both of these values are less than 0.05 so that based on this test, there is a significant difference in giving infusion or turmeric juice to the growth of Staphylococcus colonies of aureus.

Table 4.5 Pearson Correlation Test the effect of infusion and turmeric oarding on the Staphylococcus aureus growth

Treatment group	Significance
Giving turmeric infusion	.002
Giving turmeric infusion	.000

Based on table 4.5, it appears that the significance value of turmeric infusion on the growth of staphylococcus aureus colonies is 0.002 and the significance value of giving turmeric juice on the growth of

staphylococcus colonies is 0.000, this value is lower than 0.05, so it can be concluded that there is a significant correlation to the growth of staphylococcus aureus colonies in administration of doses acting on infusion and turmeric juice.

Discussion

The effect of turmeric infusion on the Staphylococcus aureus growth

Based on the results of this research which can be seen in table 4.4, it can be seen that there is a significant difference in the administration of turmeric infusion on the Staphylococcus aureus growth.

Staphylococcus aureus is a gram positive cocci bacteria. Gram positive bacteria have only single plasma membrane surrounded by thick cell wall of the peptidoglycan. Nearly 90% of the cell walls of these gram-positive bacteria are composed of peptidoglycan.

The chemical compounds of turmeric rhizome with water solvents include alkaloids, tannins, flavonoids, glycosides and carbohydrates (Gupta et al., 2015). Flavonoids can interfere with cell wall formation with peptidoglycan transpeptidase activity which will break down cell walls and damage cell membranes so that important components such as proteins, nucleic acids and nucleotides will be lysis (Dewi, 2015). According to Çıkrıkçı et al (2008) curcumin is a phenolic compound that can inhibit bacterial growth by denaturing and damaging cell membranes so that metabolic processes are disrupted.

The infusion process is the process of heating natural ingredients at the temperature of 90^0 C for 15 minutes with the aim of removing the active substances contained in these ingredients

Table 4.5 shows that there is a significant correlation to the growth of staphylococcus aureus at 10%, 30% and 50% incremental doses of turmeric infusion. Antimicrobials can have a concentration dependent killing, which can kill bacteria based on levels (Katzung, 2007). The higher the level of the antibiotic, the more places it binds to the bacterial cell.

The effect of giving turmeric juice on the Staphylococcus aureus growth

Based on the results, can be seen in the table 4.4, it can be seen that there is a significant difference in giving turmeric juice to the Staphylococcus aureus growth.

Staphylococcus aureus is cocci bacteria which has only a single plasma membrane surrounded by a thick cell wall of peptidoglycan. Nearly 90% of the cell walls of these gram-positive bacteria are composed of peptidoglycan.

One of the active ingredients contained in turmeric is essential oil. essential oil contains 10 sesquiterpenes which are derivatives of certain compounds which are proven to have strong antibacterial activity. Mono terpenes can diffuse into cells and damage the cell membrane structure.

Table 4.5 shows a significant correlation to the growth of Staphylococcus aureus at 10%, 30% and 50% levels of turmeric juice. Antimicrobials can kill bacteria based on levels (Katzung, 2007). The more bacteria that are exposed to high amounts of antimicrobial active substances will increase the effectiveness of the antimicrobial agent.

Conclusion

There is an effect of giving infusion and turmeric juice (*Curcuma domestica val*) on the Staphylococcus aureus growth by invitro and there is an effect of giving

multilevel doses of infusion and turmeric juice (Curcuma domestica val) on the Staphylococcus aureus growth invitro

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Pregnancy and Delivery with Cardiac Disease in Dr. Soetomo Hospital 2018

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ABSTRACT

Background: Cardiac disease is one of the non obstetric problems causing mortality both in pregnancy and labor due to the complications. Preventions for the complications have not been implemented, thus the number of patients which have cardiac disease with complications and perinatal outcome with low birth weight is still high. Objective : To identify maternal and neonatal outcome of pregnant women with cardiac disease in dr. Soetomo Surabaya hospital in 2018. Method: Descriptive retrospective study using medical records in dr. Soetomo Surabaya hospital 2018. Result: We found 1433 pregnancy cases with 51 (3,6 %) patients were having cardiac disease and included in this research. The most common maternal complication was pulmonary hypertension 16 cases. A dead case was found 1 case (1,9 %) with eissenmenger syndrome. We found the perinatal outcome of 30 babies (58.8%) born with a weight of 2500 gram and under. There are 7 patients with cardiac disease that have been corrected (13,7%). Among those 7 patients, 6 had a perinatal outcome with a birth weight of more than 2500 gram. Conclusion : Most pregnant patients with cardiac disease in dr. Soetomo Surabaya hospital 2018 are already having some complications with perinatal outcomes of low birth weight. Therefore, management of cardiac disease in pregnancy to prevent complications by means of preconception counseling, good antenatal care, and appropriate referrels are still needed to improve the quality of maternal and neonatal outcomes.

Introduction

Cardiac disease is a non-obstetric problem that lead to morbidity and mortality for both maternal and fetal due to the complications of cardiac function disorder (Ruys, *et al.*, 2013). In RSUD Dr. Soetomo Surabaya period 2014-2016, the second biggest causes of maternal death is cardiac disease, and the most cases happen is Eissenmenger syndrome.

Some studies report that the maternal outcome of cardiac disease in pregnancy is fetal growth restriction. By having an overview for maternal and fetal outcome in pregnancy with cardiac disease, the preventions of complication in pregnancy with cardiac disease are expected, also understand how to identify the Antenatal Care for patients with cardiac disease in pregnancy to improve the quality of maternal and fetal outcome (Fernandez, *et al.*, 2010) . The objective of this study is to give an overview on maternal and fetal outcome in patients with cardiac disease in pregnancy in RSUD Dr. Soetomo 2018.

Methods

This research was a descriptive retrospective research which was located in

dr. Soetomo Hospital in 2018 by using medical records. The samples were all mothers with heart disease. The inclusion criteria in this study were pregnant women with heart disease. While the exclusion criteria were pregnant women with hypertension, preeclampsia and mothers with incomplete data.

The investigated characteristics of the mothers were age, parity, arrival status, origin area of referrals, antenatal care (ANC), indication of termination, and the way of delivery. Obtained maternal outcomes were cardiac complications, obstetric complications, and maternal mortality. While the Obtained fetal outcomes were birthweight, Apgar score, complications and fetal mortality.

Result

Search data on medical records was succeeded in getting 1433 women who Gave birth in 2018. Some 67 of them were pregnant women with heart disease. We sorted them According to inclusion criteria. The total number of pregnant women who met the criteria were 51 women.

Table 1. Distribution of pregnant Patients with heart disease in 2018 based on age Patients

Characteristics	amount	Precentage (%)
Mean age (years old)	28.6	
Youngest (years old)	20	
Oldest (years old)	44	
< 20 years old	0	0
20-30 years old	31	60.8 %
> 30-40 years old	18	35.3 %
> 40 years old	2	3.9 %
Gestational Age		
Multigravida	28	54.9%
Primigravida	23	45.1%

Source: secondary data (Medical Record on Emergency Departement and Policlinic of RSUD Soetomo)

At the time of delivery, gestational age of <20 weeks were 1 case (1.9%), 20 weeks were less than 37 weeks were 24 cases (47.1%) and > 37 weeks were 26 cases (51.0 %).

Tabel 2. Prevalence of Heart Disease in Pregnancy at Dr. Regional Soetomo General Hospital in 2018

Characteristics	Total
Had heart disease	
Yes	51(3.6%)
No	1382(96.4%)
Type of Heart Disease	
Congenital	22(43.1%)
Acquired	13(25.5%)
PPCM	16(31.4%)

Source: secondary data (Medical Record on Emergency Departement and Policlinic of RSUD Soetomo)

The most common congenital heart disease was ASD, 13 Patients (25.5%), Followed by 4 Patients of VSD (7.8%), 2 Patients of PDA (3.9%), 1 patient had TOF (1.9%), and 1 patient with ASD and VSD (1.9%)) and 1 patient with PDA and VSD (1.9%). For acquired heart disease, RHD was dominated by 13 Patients (25.5%) and coronary heart disease was not obtained during 2018. The number of pregnant women with RHD during 2018 were 13 women. Involvement of more than one valve (multiple valve), there were 11 cases (84.6%) while single valve were only 2 cases.

The mitral valve is a valve that is often found to have damage in RHD at pregnancy women. From our data there were 7 cases of mitral regurgitation (53.8%), 2 cases of mitral stenosis (15.4%) and 2 cases of mitral stenosis-regurgitation (15.4%).

Tabel 3. Cardiac and Obstetric Complications in Pregnant Patients with Heart Disease at Dr. Soetomo Regional General Hospital in 2018

characteristic	Amount
cardiac complication	
DCFC	15
pulmonary edema	6
Eisenmenger syndrome	4
PHT	16
AF	2
obstetric complication	

PROM	4
placenta Previa	1
BSC	4
Obesity	8
Severe Oligohydramnios	7
fetal malpresentation	5
fetal Distress	10
SC indication	
placenta Previa	1
BSC	4
Class III obesity	8
Severe oligohydramnios	7
fetal distress	10
fetal malpresentation	5
perinatal complication	
perinatal mortality	9
low Birthweight	18
IUGR	6
Preterm	24
Abortion	1

Source: secondary data (Medical Record on Emergency Departement and Policlinic of RSUD Soetomo)

In Patients with acquired cardiac disease, ASD defects <2 cm were Obtained in 6 cases (42.8%),> 2 cm in 7 cases (50%), post ASO in 1 case (7.1%). VSD ≤ 1cm defects were 2 cases (33.3%), VSD defects> 1 cm were 4 cases (66.7%). Complications of ASD defects> 2 cm that occur include IPM were 5 cases, pulmonary edema was 1 case, DCFC was 1 case, Eisenmenger were 3 cases. Whereas ASD defects <2 cm included HDI were 2 cases and DCFC was 1 case. Complications of VSD defects> 1 cm include HDI was 1 case, DCFC was 1 case, eisenmeinger was 1 case. Complications of VSD defect ≤ 1 cm were 2 cases include PHT, DCFC was 1 case.

Based on the mode of delivery in pregnant patients with heart disease, predominantly labor perabdominam 30 cases (59%) and vaginal many as 20 cases (39%) and least curettage 1 case (2%). Indications of SC for heart disease in pregnancy were dominated by fetal distress in 10 cases, Followed by the class III obesity were 8 cases, severe oligohydramnios were 7 cases, fetal malpresentation were 5 cases, BSC were 4 cases, Eisenmenger syndrome were 4 cases, Pulmonary edema were 2 cases, placenta previa was 1 case, IUGR were 6 cases, and abortion was 1 case. From birth perabdominam, who performed the action B-Lynch as much as 6 cases (22%), while that does not do the B-Lynch 24 cases (78%). Of vaginal delivery, which do painless labor as many as 13 cases (76%), do not painless labor as much as 4 cases (24%). From persainan vaginal, spontaneous back of the head 7 cases (13.7%), while those with forceps extraction of 13 (25.5%).

Table 4. Pregnancy with Heart Disease in 2018 based on Antenatal Care (ANC) and referral

characteristic	**Amount**
Community Healt Center	1 (1.96%)
PH 1	16 (31.37%)
Hospital inside of Surabaya city	5 (9.80%)
Hospital ouside of Surabaya city	23 (45.09%)
Come by Her self	6 (11.76%)

Source: secondary data (Medical Record on Emergency Departement and Policlinic of RSUD Soetomo)

From all cases of pregnancy with cardiac disease in RSUD dr. Soetomo, mostly are non booked case (NBC) which is 18 caes (35,5 %). The booked case from Policlinic are 16 cases (31,37%), and the last 17 cases (33%) are from outside RSUD dr. Soetomo Surabaya.

Based on the ANC of pregnant Patients with complications of cardiac diseases, there were 4 cases (7.8%) in Patients who had never had the ANC were not Obtained DCFC> class II, it was Obtained DCC> class II as many as 1 case (1.9 %), with the number of pregnant Patients with heart disease were that the ANC had never had as many as five cases (9.8%). In Patients with ANC as many as 1-4 times during pregnancy, there were no complications of DCFC> class II in 24 cases (47.0%), while Reviews those who Obtained DCFC complications> class II were 6 cases (11.8%). The total number of pregnant Patients with cardiac disease, with 1-4 times Reviews their ANC during pregnancy as many as 30 cases (58.8%). Patients with ANC> 4 times who did not have DCFC> Class II complications were 14 cases (27.5%), while Reviews those who Obtained DCFC complications> Class II

were 2 cases (3.9%). The total number of ANC Patients> 4 x who did not get DCFC> class II were 14 cases (27.5%), while Reviews those who Obtained DCFC> class II were 2 cases (3.9%). While the total number of Patients with ANC> 4 times were 16 cases (31.3%). Of all 51 Patients, 42 cases (82.4%) were found in DCFC> class II and 9 cases (17.6%).

Based on ANC correlation of pregnant patients with PHT complications, there were 3 patients (5.9%) who had never had ANC and did not have complications of PHT, while severe PHT were 2 cases (3.9%). The number of patients who had never had ANC were 5 cases (9.8%). Patients who had 1-4 times of ANC, and did not have complications of PHT were 19 cases (37.6%), mild PHT were 2 cases (3.9%), moderate PHT were 4 cases (7.8%), severe PHT were 5 cases (9.8%). The total number of patients with ANC were 30 cases (58.8%). Patients with ANC> 4 times and did not have PHT were 12 cases (23.5%), mild PHT was 1 case (1.9%), moderate PHT were 2 cases (3.9%), severe PHT was 1 case (1.9%). Total patients with ANC> 4 times were 16 cases (31.3%).

There is one case of death of pregnant patients with heart disease in 2018 with secundum ASD sekundum R to L shunt + Severe PHT + Eissenmenger Syndrom + moderate TR + mild PR. The patient is reffered from RSUD Nganjuk and never come to RSUD dr. Soetomo Surabaya before.

There are 7 pregnant Patients with heart disease, post-correction in 2018, that have a better maternal and perinatal outcome compared with uncorrected cardiac disease in pregnancy (Yap, *et al.*, 2010).

Most babies with heart disease mother was born at term> 2500 g were 21 cases (41.2%). Babies weighing 1501-2500 g of 20 cases (39.2%), while from 1001 to 1500 g as 6 cases (11.8%) and <1000 g of as much as 4 cases (7.8%)

Fetal outcomes for pregnant Patients with heart disease were mostly mild or without asphyxia asphyxia in 38 cases (74%). While moderate asphyxia were 9 cases (18%), severe affixia was 1 case (2%), IUFD were cases (6%).

Discussion

Based on the number of parity, cardiac disease found in multigravida more than primigravida. It shows that family planning hasn't working optimally in Indonesia. Most patients diagnosed with cardiac disease in the next pregnancy, because the in the first pregnancy, no signs and symptoms are shown and there is no complications. In the next pregnancy signs and symptoms are shown because maternal adaptation is not optimal (Gumilar and Pradyani, 2020).

Table 5. Characteristics of Pregnant Patients with Post Correction Heart Disease in 2018

No / name / Age (years old)	parity	Type of Heart Disease	Valve involvement	Cardiac complication	Obstetric complication	MOD	Fetal outcomes	Gestational age	Contraception	ANC
1 Mrs. S / 30	Multi	Post MVR	Severe wi MS	Mild PHT	Category II NST	SC	P / 3000 g / 50 cm / USA 8-9	39/40	Sterilization	PH1> 4x
2 Mrs. K / 28	Primi	Post MVR bioprosthetic	Severe wi MS	Increased tension of the mitral valve,	-	SC	L / 3300 g / 49 cm / USA 8-9	38/39	IUD	PH1> 4x
3 Mrs.P / 30	Multi	Post MVR mechanical valve prostetic	Severe wi MS	Mild IPM, AF	-	FE + painless labor	L / 3000g / 51cm / USA 8-9	38/39	IUD	PH1> 4x
4 Mrs.I / 22	Primi	Post DVR	PDA	Mitral + Aorta (MS + AR)	-	FE + painless labor	L / 2900g / 49 cm / AS8-9	37/38	IUD	PH1> 4x
5 Mrs.E / 24	Multi	Post correction TOF	TR, TOF	-	-	FE + painless labor	P / 3600 g / 51 cm / USA 8-9	38/39	IUD	RS wiliam booth
6 Mrs.Pi / 22	Primi	Post ASO	ASD L to R shunt	-	fetal distress	SC + B-Lynch	P / 3400 g / 50 cm / USA 5-7	38	IUD	PH1> 4x
7 Mrs.N / 35	Multi	Post MVR	Severe ai MS	-	IUFD	Pliers muxeoux + painless labor	P / 2200g / 40cm / AS0 / meconeal	34/35	-	Bangkalan Hospital

Source: secondary data (Medical Record on Emergency Departement and Policlinic of RSUD Soetomo)

Most of the pregnant patients with cardiac disase in RSUD dr. Soetomo 2018 are having cardiac complications. DCFC and PHT is the most complications cases in pregnancy, PHT is 16 cases and DCFC 15 cases. A study conducted in Vietnam in 2014-2016 by Thang Nguyen Manh shows that the most cardiac complication in pregnancy is arrythmia, which is 55 cases among 284 patients with cardiac disease (19,4 %) (Nguyen Mahn, *et al.,* 2019). ANC frequency on pastients with PHT and DCFC is not significantly associated. It shows that the quality of ANC needs to consider as associated with the prevalence of cardiac and obstetric complications. During pregnancy, the regularity of ANC in Policlinic is needed to monitor the maternal and fetal condition.

The pregnant patients with cardiac disease post correction shown low in number, among 51 patients, there are only 7 patients are being corrected. The fetal outcome of 6 among 7 patients that being corrected is good, with fetal birth weight is more than 2500 g. It shows that cardiac correction is significant to decrease the complications in maternal and fetal (Bills, *et al.,* 2018). Otherwise in primigravida patients with cardiac disease that are not allowed to be pregnant before correction shows that preconceptional counseling is not optimal. Precoceptional counselling is very important in patients with among reproductive age with cardiac disease (Iserine, 2001). Counseling are given as needed for the patient to know the risk on the pregnancy. Informations needs to be given completely for the patients to understand the prognosis of the pregnancy and the baby (Gumilar and Pradyani, 2020). Perinatal outcome found 30 babies (58,8 %) are born with low birth weight ≤ 2500 g, it also found in the study conducted in Vietnam period 2014-2016 by Thang Nguyen Manh, the perinatal outcome IUGR found 26 among 284 cases (9,2%) (Nguyen Manh, *et al.,* 2019).

A death case is found in patients with cardiac disease in 2018 due to complications which is Eissenmenger syndrome (Regitz-Zagrosek, *et al.,* 2018). The patient is referred from outside Surabaya and have never come to Policlinic in RSUD dr. Soetomo Surabaya. The patients came in a poor conditions and having an advanced underlying disease is the causes of the death (Wolfe, *et al.,* 2019). Late refferal shows that the ANC and management of patients with cardiac disease is not optimal yet (Gumilar and Pradyani, 2020).

Conclusion

Most of the pregnant patients with cardiac disease in RSUD dr. Soetomo Surabaya in 2018 are having cardiac complications with perinatal outcome low birth weight. Thus, the integrated management needs to be conducted since the preconceptional care until post partum to prevent the complications by preconceptional counseling, screening, antenatal care, and refferal on time to improve the maternal and fetal outcome.

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Host Immune Response To Malaria

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ABSTRACT

Malaria is still a health threat, especially for children and pregnant women in endemic areas. The World Health Organization (WHO) reports 228 million cases of malaria occur worldwide and an estimated 405,000 deaths from malaria globally in 2018. A series of malaria control efforts according to WHO recommendations have been carried out widely. However, these programs face obstacles. Therefore, the existence of an effective malaria vaccine is absolutely necessary in a series of malaria control strategies. Development of a malaria vaccine requires a basic concept regarding the host's immune response to malaria. Unfortunately, only a few in Indonesia have reviewed how the immune response is. This article will present an understanding of how the human immune system responds to *Plasmodium falciparum.*

Introduction

Until now, malaria is still a health problem, especially for children and pregnant women in endemic areas. The World Health Organization (WHO, 2019) reports 228 million cases of malaria occur worldwide and an estimated 405,000 deaths from malaria globally in 2018. Most malaria deaths occur in children younger than five years in Africa and accounted for 67% (272,000) of all deaths from malaria worldwide. Malaria is an endemic disease in several countries in the world including Indonesia.

In 2018 there were 28 high endemic districts / cities from 4 provinces, namely Papua, West Papua, NTT and East Kalimantan (Kemenkes, 2018). According to Riskesdas in 2010, malaria caused by *Plasmodium falciparum* had a prevalence of 86.4% and was the highest prevalence in among all types of malaria (Kemenkes, 2011).

In addition to having a high mortality and prevalence rate, falciparum malaria also has a high rate of morbidity and progression. A series of malaria control efforts according to WHO recommendations have been carried out extensively, including prevention with Long-Lasting Insecticidal Nets (LLIN), vector control with Indoor Residual Spraying (IRS), and treatment with Artemisinin-based Combination Therapy (ACT). However, these programs face obstacles, including the spread and increase in the number of parasites that are resistant to antimalarial drugs and vectors that are resistant to insecticides. Therefore, the existence of an effective malaria vaccine is absolutely necessary in a series of malaria control

strategies, in addition to existing effort (Nindela, 2015).

Development of malaria vaccines has been ongoing for more than six decades, but until now there has been no vaccine that has been licensed. The main challenge in developing an effective malaria vaccine is the ability to provide protection against various forms of malaria parasites. caused by complex life cycles with various antigens expressed at each stage. Another major challenge is understanding minimal interactions between parasites and human immune mechanisms (Hill, 2011).

Because malaria parasites are very complex, the direction of vaccine development is carried out with several different approaches. Early in the development of the vaccine, efforts were made to focus on the pre-erythrocyte phase, namely the parasitic period in the form of sporozoites that enter the blood vessels and into the liver, which then progresses to maturity and begins the multiplication process (Douradinha, 2011). The following review will discuss the life cycle malaria parasites and immune response mechanisms against malaria infections.

Malaria

Malaria is a disease caused by intracellular obligate parasitic infection (protozoa) of the genus plasmodium which can be transmitted by the bite of an infected female Anopheles mosquito parasite (vector borne disease). This disease is usually characterized by fever, anemia, and hepatosplenomegaly. Malaria can attack anyone, especially residents who live in areas where the place is a place that suits the needs of mosquitoes to develop (Arsunan, 2012).

There are five species of plasmodium that can cause malaria in humans, namely *Plasmodium falciparum (P. falciparum), Plasmodium vivax (P. vivax), Plasmodium ovale (P. ovale), Plasmodium malariae (P. malariae),* and *Plasmodium knowlesi (P. knowlesi)*. But according to WHO, species that are often found and become a global focus are *P. falciparum and P. vivax*. In 2018, *P. falciparum* accounted for 99.7% of malaria cases in Africa, 50% of cases in Southeast Asia, 71% of cases in the Eastern Mediterranean, and 65% in the Western Pacific. Whereas *P. vivax* is the main parasite in the American region as much as 75% (WHO, 2019).

For survival, all species of malaria parasites basically require two types of life cycles, namely the sexual / sporogony cycle, the cycle in the mosquito body and the asexual / schizogony cycle, the cycle in the human body. Each stage of parasitic development is characterized by differences in antigen expression. Therefore understanding the life cycle of the malaria parasite is the basis for efforts to develop a malaria vaccine. The development of parasites as well as the interactions of parasites and their hosts determine the severity and pathogenesis of the disease clinically (Ballou, 2005).

Asexual Cycle (Schizogony)

When female Anopheles mosquitoes are infective inhaling human blood, sporozoites in the salivary glands will enter the bloodstream for about half an hour. After that, sporozoites will enter the liver cells and develop into liver schizons consisting of 10,000-30,000 liver merozoites (depending on the species). This cycle is called the eco-erythrocyte cycle which lasts for approximately 2 weeks. In *P. vivax and P. ovale*, after

sporozoites enter they do not develop directly into schizons, but some form dormant forms called hypnozoites. The hypnozoites can stay in the liver cells for months to years. At some point when the body's immunity decreases, it will become active so that it can cause a recurrence or recurrence (long term relapse) (CDC, 2019).

Merozoites originating from broken liver schizons will enter the bloodstream and infect red blood cells. In red blood cells, the parasite develops from the trophozoite stage to schizon (8-30 merozoites, depending on the species). Furthermore, infected erythrocytes (skizons) rupture and merozoites that come out will infect other red blood cells. This cycle is called the erythrocyte cycle. Each broken erythrocyte schizon will produce 6 - 32 merozoites which will infect new erythrocytes and start the cycle again. The number of erythrocytes lysis is one of the causes of anemia. After several generations of merozoites are formed, some of them grow into sexual forms that are gametocytes (gamete stem cells). The shape of gametocytes varies in each species of malaria parasite (Krattigen, 2006).

Sexual Cycle (Sporogony)

Mosquitoes will be infected with malaria when sucking the blood of patients who contain gametocytes. When mosquitoes suck the blood of patients, gametocytes carried in the blood will then undergo the process of maturation into male and female gametes in the gut of mosquitoes. Both types of gametes then unite to produce ookinet, ookinet moves to penetrate into the outer intestinal wall and experience maturation into oocysts. Furthermore oocysts will undergo meiotic division into sporocysts that contain thousands of sporozoites. These sporozoites are infective and are ready to be transmitted to humans. Based on the parasite life cycle there are 3 fundamental targets for developing a malaria vaccine, namely; pre-erythrocytic phase (sporozoit, liver stage), asexual erythrocytic and sexual phase (Targett, 2005).

Host Immune Response To Malaria

Immune responses to parasitic life cycle stages (stage specific), are divided into 3 namely:

Immune response at the Eksoeritrositer Stadium

The immune response at this stage is the immune response to the sporozoite and intrahepatic stages. The immune response at the sporozoite stage is antibodies that inhibit the entry of sporozoites into the hepatocytes. Sporozoites stimulate B cells to produce antibodies through Th2 cell intermediaries. Th2 cells will produce IL-4 and IL-5 which stimulate the formation of antibodies by B cells. The reaction of antibodies with this stage causes neutralization and opsonization occurs in phagocytic cells such as macrophages. Stimulated macrophages trigger the release of IL-12 which then activates Th1 cells. Th1 cells produce pro-inflammatory cytokines such as IL-2, IFN-gamma, and TNF a which can stimulate macrophages and other phagocytic cells.14,15 The immune response at the intrahepatic stage is mainly caused by CDC Tc cells. Sporozoites associated with dendritic cells activate Th cells which then produce IFN-gamma and activate Tc cells to destroy infected hepatocytes directly or indirectly

through IFNgamma secretion and NO (Hidayati, 2003).

Immune Response in Erythrocyte Stadium

The immune response at this stage is in the form of antibodies and phagocyte activation by Th cells. These antibodies function to agglutinate merozoites, block the entry of merozoites into erythrocytes, and kill infected erythrocytes (Riley, 2019). Infected erythrocytes will be captured by dendritic cells or macrophages which then release IL-12 will activate naive T cells into Th1 and then produce IFN- gamma. In addition, Th 1 produces IL-2 to stimulate NK cells which in turn will produce gamma IFN. The gamma IFN will then stimulate the action of cell dendritic and macrophages. On the other hand Th1 will help B cells to form antibodies. These antibodies will bind to parasites that come out of the blood and carry out opsonization (Stevenson, 2007).

Immune Response to the Sexual Stadium

The immune response at this stage is in the form of antibodies that inhibit the development of gametocytes in humans and inhibit the fertilization of gametes in mosquito vectors, inhibiting zygote transformation into the next stage before being smoked by mosquito vectors. Antibodies cause opsonization of macrophage cells (Draper, 2018).

Conclusion

Malaria is a disease caused by intracellular obligate parasitic (protozoa) infections of the genus plasmodium that can be transmitted by the bite of an infected female Anopheles mosquito parasite (vector borne disease). The Plasmodium life cycle consists of asexual (schizogoni) and sexual cycles (sporogoni). The immune response to the stage of the parasitic life cycle (stage specific) depends on the stage of eksoeritrositer, erythrocytes, and sexual stage). After understanding the basic immunology of the host response to malaria, it is hoped that vaccine development will be better.

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The Effect of Mercury Exposure to *Escherichia Coli* Bacteria Resistant to Mercury and *Escerichia Coli* Esbl in Vitro

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ABSTRACT

Background: The level of pollution in Indonesia is still very high, consist of water pollution, air pollution and soil pollution. Mercury is one of the heavy metals that pollutes the waters of the sea, while *Escherichia coli* is exposed to mercury will try to defend itself by doing mercury detoxification so that it can live in an environment that contains mercury. *Escherichia coli* that tries to defend itself from mercury exposure in the environment will experience a change in its genes into mercury resistant *Escherichia coli*. In plasmids or transposons, it might also stimulate the formation of resistance genes for some antibiotics, include producing the ESBL enzyme, so that it can convert non ESBL *Escherichia coli* into ESBL *Escherichia coli*. **Objective**: This study aims to prove that the repeated exposure of mercury will change non ESBL-mercury sensitive *Escherichia coli* into ESBL- mercury resistant *Escherichia coli*. **Method:** This was an experimental study with 27 non-ESBL *Escherichia coli* isolates as identified from Phoenix. Non-ESBL *Escherichia coli* clinical isolates were tested by giving exposure to HgCl2 with concentrations of 0.02 ppm, 0.10 ppm, 0.20 ppm for 1-14 days until mercury resistant *Escherichia coli* was formed, and then ESBL screening was tested by giving *Cefotaxime* exposure to them. **Results:** On the first day of mercury exposure, there were 9 isolates of 0.02 ppm HgCl2 resistant *Escherichia coli*, 9 isolates of 0.10 ppm HgCl2 resistant *Escherichia coli*, 9 isolates of 0.20 ppm HgCl2 resistant *Escherichia coli*. Furthermore, this *Escherichia coli* isolate was exposed to *Cefotaxim* as ESBL screening. The final results of post-exposure HgCl2 0.02 ppm was obtained 3 (33.3%) isolates were still sensitive to *Cefotaxime* and 6 (66.7%) isolates that were resistant to *Cefotaxime*. The final results of post-exposure HgCl2 0.10 ppm was obtained all 9 (100%) isolates that were resistant to *Cefotaxime*. The final results of post-exposure HgCl2 0.20 ppm obtained 2 (22.2%) isolates were still sensitive to *Cefotaxime* and 7 (77.8%) isolate were resistant to *Cefotaxime*. **Conclusion:** *Escherichia coli* in urine had the phenotive change into mercury resistant *Escherichia coli*. Mercury exposure of 0.02 ppm, 0.10 ppm, 0.20 ppm for 1 day in vitro on isolates of non ESBL-mercury resistant *Escherichia coli* caused changes in 22 isolates of *Escherichia coli* in urine.

Introduction

The level of pollution in Indonesia is still very high in the form of water, air, and soil pollution. This pollution will be a serious threat to the Indonesian state with all its potential. Humans can be exposed to mercury not only from environmental pollution but can also be caused by the use of cosmetic ingredients containing mercury, consuming food/drinks containing mercury, or due to direct contact with materials containing mercury (Saraswati and Fahruddin, 2012)

One of these wastes is that heavy metals can be sourced from factories or industries. The toxic and dangerous properties of heavy metals are shown by the physical and chemical properties of the material, both in terms of quality and quantity. Mercury is a heavy metal that pollutes marine waters, caused by natural factors and human activities that dispose of its waste into the waters. Sources of mercury waste can come from the cosmetics industry, electronics, paint manufacturing industry, denture manufacturing, gold smelting, as a catalyst, and others (Palar, 2008).

Several researchers have researched the presence of antibiotic-resistant bacteria coexisting in mercury-resistant bacteria. One of the studies that have been carried out in the research that has been conducted by Ririn (2013) from the Biology Department, Faculty of Mathematics and Natural Sciences, Hasanuddin University, Makassar. In her research, the isolation of bacteria from seawater samples from Losari Beach was carried out using Nutrient Media for Synthetic Sea Water Agar (NA ALS) added with HgCl with a concentration level of 0.0002 mg/ml (0.02µg / ml). Then the bacterial isolates were tested for antibiotic resistance using antibiotic paper disks (Oxoid) including *Ampicillin* 10µg, *Novobiocyn* 30µg, *Chloramphenicol* 30µg, *Cefoperazone* 75µg, and *Ofloxacin* 5µg. Three types of isolates are mercury (Hg) resistant and the antibiotics obtained are: mercury I resistant bacteria isolates which are also resistant to *Ofloxacin* 5µg, mercury II resistant bacteria isolates that are resistant to *Ampicillin* 10µg and mercury III resistant bacteria isolate that is resistant to all types of antibiotics (Ririn, 2013).

Bacteria exposed to mercury will try to defend themselves by detoxifying mercury, so that these bacteria can live in environments that contain mercury. Bacteria that try to defend themselves from exposure to mercury in the environment will experience a change in their genes to become mercury-resistant bacteria. Mercury detoxification by mercury-resistant bacteria occurs because bacteria have the *mer operon gene* (Boyd, 2012).

The structure of the operon mer is different for each type of bacteria. Generally, the operon mer structure consists of the metalloregulator gene (merR), the mercury transfer gene (merT, merP, merC), the mercury reductase gene (merA), and the organo mercury lyase (merB). Bacteria that only have the mercury reductase (merA) gene are called narrow spectrum mercury-resistant bacteria. Several bacteria have in addition to the merA gene, also the merB gene, so these bacteria are called broad-spectrum mercury resistant bacteria. The protein merA gene is responsible for the presence of the enzyme mercury reductase. The mercury reductase enzyme will give 2 electrons to NADPH or NADP so Hg2 + turns into Hg0 which is volatile and will be removed from the cell, while the MerB protein has the function of catalyzing the breaking of the mercury-carbon bond so that organic compounds and Hg2 + ions are produced. (Barkay et al., 2003).

In plasmids or transposons, it may also stimulate the formation of genes coding for resistance to several antibiotics, one of which is the enzyme-producing bacteria ESBL, where ESBL is mostly derived from the TEM and SHV enzymes, and in lesser amounts than CTX (Walker, 2015) where the ESBL coding gene can be either chromosomal or plasmidal. Changes in *E. coli* were initially sensitive to mercury without ESBL, but because they live in an environment that has high mercury levels, it can change to ESBL mercury-resistant *E.*

coli. This is what makes researchers feel the need to do this research because with a large amount of mercury that is in nature, both in the environment, including air, soil, water, besides that there are animals that have been contaminated with mercury that we consume, many of the items we use are used. contains mercury ranging from cosmetics, medical equipment, factories, etc. and if we are exposed to these items then we will be contaminated with the mercury material and then the mercury levels in our bodies will be high. If there are bacteria that enter our bodies, then there is a possibility that bacteria are initially sensitive to non-ESBL mercury will become resistant to ESBL mercury, which is very dangerous for us and complicates the treatment.

In this study, the researchers researched bacteria that were resistant to mercury (Hg) and ESBL whose isolates were taken from urine specimens at the Clinical Microbiology Unit of Dr. Soetomo Hospital, Surabaya.

Methods

This research is an experimental study, by providing treatment and observation of the results of urine culture that grows mercury susceptible non-ESBL *E. coli* bacteria. The *E. coli* strain is a clinical urine isolate stored in the Clinical Microbiology Unit of the Dr. Soetomo Hospital, Surabaya.

The study population was clinical isolates of *E. coli* stored from urine specimens in the Clinical Microbiology Unit of Dr. Soetomo Hospital, Surabaya. The sample of this study was clinical isolate *E. coli* non ESBL stored from urine specimens in the Clinical Microbiology Unit of Dr. Soetomo Hospital, Surabaya. ppm to non-ESBL *E. coli* bacteria for 1-14 days.

The number of samples needed in this study is:

$(r-1)\ (t-1) \geq 15$
$(r-1)\ (3-1) \geq 15$
$(r-1)\ (2)) \geq 15$
$(r-1) \geq 3$
$r \sim 9$

Information :
r = total samples
t = total treatment

So this study used 9 isolates of *E. coli* susceptible mercury non ESBL.

The Sample's Criteria

Inclusion criteria: *E. coli* comes from urine specimens in the Clinical Microbiology Unit of Dr. Soetomo Hospital and the *E. coli* isolate was not ESBL *E. coli* based on the identification and sensitivity testing with Phoenix or Vitex 2. Exclusion

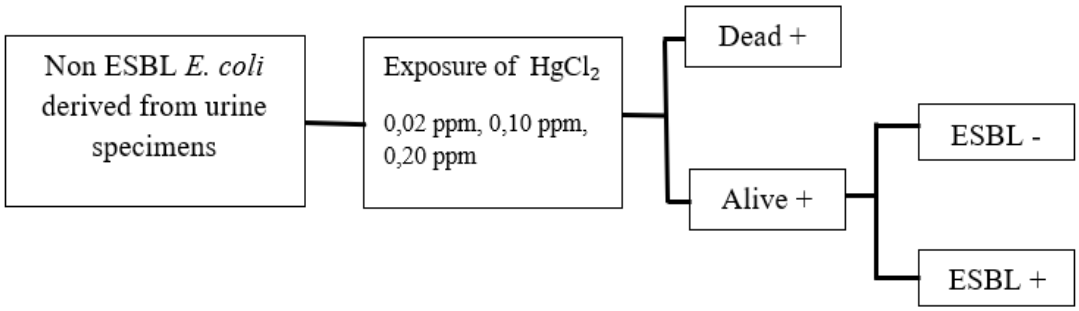

Figure 1. Research Diagram

criteria: stored *E. coli* isolates that do not grow.

Sampling Technique

A sampling of stored clinical *E. coli* isolates from urine specimens in the Clinical Microbiology Unit, was carried out using consecutive sampling techniques. Each sample that meets the research criteria is taken for the required sample size.

Research Variables And Operational Definitions

Research Variables

1. Independent Variables: Repeated exposure of $HgCl_2$ in 0,02 ppm, 0,10 ppm, and 0,20 ppm for 1 - 14 days
2. Dependent Variables: Occurence of *E.coli* resistence Mercury and which categorized as ESBL produce

The research was conducted at the Clinical Microbiology Unit of Dr. Soetomo Hospital, Surabaya. From May 2019 - August 2019. The main material used in this study was clinical isolates of *E. coli* bacteria non ESBL stored from urine specimens in the Clinical Microbiology Unit Dr. Soetomo Surabaya. Additional materials used in this study were Mueller-Hinton agar, $HgCl_2$ liquid with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm, 30µg *Cefotaxim*e antibiotic disk.

Difusion Method

The Techniques That Used In Laboratory

1. The media was used is MHA (Mueller-Hilton Agar)
2. Empty disc which dropped by $HgCl_2$ liquid with 0,02 ppm, 0,10 ppm, and 0,20 ppm consentration

The Procedure:

1. Do the streaking of the bacteria that will be tested on all surfaces so that they are evenly distributed.
2. Place an empty disc dripped with liquid HgCl with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm on the agar surface.
3. Plate 9-10 cm in diameter.
4. Furthermore, the plates were incubated at 35 ° C for 24 hours.
5. The zone diameter is measured in mm.

The Interpretation Result Of Treatmented *E. coli*

1. Susceptible (S)
   The tested isolate can be inhibited with this antimicrobial at the recommended dosage. It is said to be susceptible if an inhibition zone is obtained.
2. Resistance (R)
   This means that isolates cannot be inhibited by these antimicrobials. It is said to be resistant if an inhibition zone is not found.

Research Work Procedure

Mercury Disc Preparation

a. $HgCl_2$ disc 0,02 ppm consentration is a mercury which diluted with Cl_2.
b. $HgCl_2$ disc 0,10 ppm consentration is a mercury which diluted with Cl_2.
c. $HgCl_2$ disc 0,20 ppm consentration is a mercury which diluted with Cl_2.

Bacteria Isolate Preparation

1. *E. coli* isolates stored from urine specimens in the Clinical Microbiology Unit have been identified and tested for antibiotic sensitivity.
2. Isolates that met the criteria as *E. coli* bacteria and the degree of sensitivity to *Cefotaxim*e, Ceftazidime, Ceftriaxone, and Aztreonam (Phoenix-BD, CLSI M100-S 2019) were selected 3 - 5 colonies from MacConkey agar media using cotton stick swabs.

3. Then it is suspended in a 0.9% NaCl solution in a glass tube until it reaches a germ density of 0.5 McFarland which is equivalent to 1.5 x 108 CFU / mL.

Hg Disc and *Cefotaxim*e Preparation

1. The 0.5 McFarland suspension was densely planted onto the MHA surface. Placed the disc which already dripped by $HgCl_2$ with 0,02 ppm, 0,10 ppm, and 0,20 ppm consentration in the surface of MHA.
2. MHA plates were incubated for 18-24 hours at 35 ° C ± 2 ° C.

Isolate Preparation for 2 Days of Exposure and Later

1. Colonies that are on the edge of the inhibition zone are taken with a sterile cotton swab
2. Then it was suspended in a 0.9% NaCl solution to reach 0.5 McFarland turbidity.
3. The 0.5 McFarland suspension was densely planted onto the MHA surface. On the surface of the MHA, a disc that has been dripped with HgCl is placed with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm
4. MHA plates were incubated for 18-24 hours at 35 ° C ± 2 ° C.

Read The Sensitivity Test of *Gentamycin* and CTX

1. The sensitivity test to $HgCl_2$ is said to be susceptible if the diameter of the zone of inhibition is ≥ 15mm, and resistant if ≤ 12mm.
2. The sensitivity test to *Cefotaxim*e is said to be susceptible if the zone of inhibition is ≥ 26mm and resistant if the zone of inhibition is ≤ 22mm
3. The ESBL screening test is said to be positive if it is resistant to *Cefotaxime*

Reasearch Data Collection Procedures

The research data collection procedure consisted of observing and recording the results of the observations into the table that had been provided.

Data Processing and Analysis Techniques

Processing techniques and data analysis were obtained statistically using Chi-square analysis.

Result

The samples of this study were 27 *Escherichia coli* isolates obtained from clinical specimens taken by consecutive sampling. Samples were collected from May 2019 to August 2019. *E. coli* isolates obtained from the phoenix automatic machine were retested using the Kirby-Bauer method, the results are in table 5.01. The re-sensitivity test using the Kirby-Bauer antibiotic disc diffusion method was carried out to equate the methods used during the screening test and ESBL confirmation.

All isolates that met the inclusion-exclusion criteria were exposed to $HgCl_2$ at concentrations of 0.02 ppm, 0.10 ppm, 0.20 ppm, and *Cefotaxim*e (CTX). The exposure was carried out every day in a petri dish containing Mueller Hinton Agar using $HgCl_2$ with a concentration of 0.0.02 ppm, 0.10 ppm, 0.20 ppm with a maximum length of research for 1 day. If within 1 day of the study a positive result of mercury resistance is obtained, then it will be continued by providing exposure to screen for ESBL.

The research was carried out using the Kirby-Bauer method, by dripping a blank disc with drops of $HgCl_2$ with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm then a disc containing $HgCl_2$ with a concentration of 0.02 ppm, 0.10 ppm, 0.20

ppm was exposed on the surface of the MH agar plate. After being incubated for 24 hours, the results are in the following table. The basis for determining the concentration of mercury used in this study is based on research conducted by Natalia from Unair, which resulted in a mercury concentration of 1.22 ppm *E. coli* bacteria were still alive. So the researchers used mercury with a concentration of 0.02 ppm, 0.10 ppm, and 0.20 ppm in the hope that researchers would get results whether in an environment containing mercury with a concentration of 0.02 ppm *E. coli* bacteria could still survive. This research technique uses the Kirby-Bauer method by dripping a blank disc with a concentration of 0.02 ppm of $HgCl_2$, 0.10 ppm, 0.20 ppm then a disk containing $HgCl_2$ with a concentration of 0.02 ppm, 0.10 ppm, 0, 20 ppm was exposed on the surface of the MH agar plate.

The method used is based on the direction of Edy Bagus who is a professor in Microbiology, Airlangga University, which is the result of his experience and research in Japan.

Table 1. *E. coli* Resistance To $Hgcl_2$ Exposure With Consentration Of 0,02 Ppm (n=9), 0,10 ppm (n=9), 0,20 ppm (n=9) by kirby-bauer method (total n=27)

No	Exposure	Exposure Day - 1	
		Sensitivity	**Resistance**
1	$HgCl_2$ 0,02 ppm	0 (0%)	9 (100%)
2	$HgCl_2$ 0,10 ppm	0 (0%)	9 (100%)
3	$HgCl_2$ 0,20 ppm	0 (0%)	9 (100%)

On the first day of exposure to $HgCl_2$ using the Kirby-Bauer method using a blank disk that has been dripped with HgCl2 with a concentration of 0.02 ppm, 9 (100%) resistant isolates were obtained, by exposure to $HgCl_2$ with a concentration of 0.10 ppm obtained 9 (100 %) isolates that were resistant and by exposure to $HgCl_2$ with a concentration of 0.20 ppm, obtained 9 (100%) resistant isolates.

The next stage of the research was carried out using the results of the first treatment, by exposure to HgCl2 concentrations of 0.02 ppm, 0.10 ppm, 0.20 ppm then exposed to the *Cefotaxime* disk as a screening for ESBL.

Tabel 2. *E. coli* Resistance to *Cefotaxime* post $HgCl_2$ Exposure in 0,02 ppm (n=9), 0,10 ppm(n=9), 0,20 ppm (n=9) Consentration with Kirby-Bauer Method (total =27)

No	Exposure	Exposure Day – 1 CTX	
		Sensitivity	**Resistance**
1	$HgCl_2$ 0,02 ppm	3 (33,3%)	6 (66,7%)
2	$HgCl_2$ 0,10 ppm	0 (0%)	9 (100%)
3	$HgCl_2$ 0,20 ppm	2 (22,2%)	7 (2,8%)

On the first day of exposure to *Cefotaxim*e on the results of 0.02 ppm HgCl2 exposure, 3 (33.3)%) isolates were still susceptible to *Cefotaxim*e and 6 (66.7%) isolates were resistant to *Cefotaxim*e. On the first day of exposure to *Cefotaxim*e on the results of exposure to HgCl2 0.10 ppm, there were no (0%) isolates that were still susceptible to *Cefotaxim*e and 9 (100%) isolates that were resistant to *Cefotaxim*e. On the first day of exposure to *Cefotaxim*e on the results of exposure to HgCl2 0.20 ppm, 2 (22.2)%) were still susceptible to *Cefotaxim*e and 7 (77.8%) isolates were resistant to *Cefotaxim*e.

All isolates from *E. coli* became resistant after exposure to $HgCl_2$ with concentrations of 0.02 ppm, 0.10 ppm, 0.20 ppm on the first day of exposure. There was no difference between exposure to $HgCl_2$ with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm. In efotaxime exposure to the emergence of ESBL in *Escherichia coli* from urine specimens, different results were obtained at each $HgCl_2$ concentration previously exposed.

Discussion

In this study, 27 isolates were exposed to HgCl2 with a concentration of 0.02 ppm (9 isolates), 0.10 ppm (9 isolates), 0.20 ppm (9 isolates), it was found that all *E. coli* isolates from urine were resistant *E. coli*. mercury. This is following research conducted by Hinonaung (2013) from the Chemistry Section of the Faculty of Medicine, Sam Ratulangi University. The research was carried out in several stages, mentioned the isolation stage of mercury resistant bacteria which aims to isolate the bacteria present in tartar, urine, and fecal samples. The results obtained from 6 isolates found four types of mercury-resistant bacteria in tartar sediment, feces, urine, there are *Enterococcus, Bacillus sp, Streptococcus sp, E. coli*. The results of the resistance test to mercury showed that 3 bacteria can survive up to a 40 ppm HgCl2 concentration, namely *Enterococcus, Bacillus sp, and Streptococcus sp*. At a concentration of 20 ppm of Phenyl Mercury, 2 bacteria can survive, namely *Bacillus sp, E.coli* (Hinonaung, 2013).

In this study, HgCl2 was used with a small concentration of 0.02 ppm to prove that with a very small concentration, *E. coli* had adapted and became mercury resistant. Heavy metal contamination, including mercury in humans, will continue to increase in line with the increasing exploitation of various natural sources where heavy metals are contained. This is related to the properties of heavy metals:

1. Difficult to degrade, so that problems accumulate in the aquatic environment and its natural presence is difficult to decompose.
2. Can accumulate in organisms and will endanger the health of humans who consume these organisms.
3. Easily accumulates in sediments, so that the concentration is always higher than the metal concentration in water. Besides, sediment is easily suspended by the movement of water masses which will dissolve the metal it contains back into the water so that the sediment becomes a potential source of pollution in a certain time scale.

Humans are exposed to heavy metals, such as mercury because the properties of heavy metals above will cause them to have mercury levels in their bodies (Widowati et al., 2008). So that the bacteria that are in the human body will be in an environment that contains mercury. Bacteria that live in environments exposed to mercury will try to defend themselves by detoxifying mercury so that these bacteria can live in environments that contain mercury. Bacteria that try to defend themselves from exposure to mercury in the environment will experience a change in their genes to become mercury-resistant bacteria.

Mercury detoxification by mercury-resistant bacteria occurs because bacteria have the *mer operon gene*. The structure of the *operon mer* is different for each type of bacteria. Generally, the operon mer structure consists of the metalloregulator gene (merR), the mercury transfer gene (merT, merP, merC), the mercury reductase gene (merA), and the organo mercury lyase (merB). Protein The merA gene is the gene responsible for the presence of the enzyme mercury reductase. The mercury reductase enzyme will give 2 electrons to NADPH or NADP so that Hg2 + turns into Hg0 which is volatile and will be removed from the cell (Brown et al, 2002), while the MerB protein has the function of catalyzing the breaking of the mercury-carbon bond resulting in organic compounds and Hg2 + ions. (Barkay et al., 2003).

However, there is another possibility besides the allegations above is that *E. coli* that enters the human body is already an *E. coli* bacteria that are already resistant to mercury. This requires further research to prove the truth of the allegations above regarding the presence of mercury-resistant *E. coli* bacteria found in the body of this research sample.

The results of the first stage were *E. coli* bacteria that had been exposed to HgCl2 with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm which turned out to be all mercury resistant, then the mercury-resistant *E. coli* bacteria were exposed to *Cefotaxime* discs for ESBL screening. Previously, *Cefotaxime* was exposed to *E. coli* on the primary plate and the results were all are *Cefotaxime* susceptible *E. coli*. After that, the *E. coli* from the primary plate was exposed to mercury with a concentration of 0.02 ppm, 0.10 ppm, 0.20 ppm, then the results of the previous exposure were exposed to *Cefotaxime* discs for ESBL screening. The results of changes in the phenotypic properties of several non-ESBL *E. coli* isolates became ESBL after being exposed to *Cefotaxime* on the first day.

On the first day of exposure to *Cefotaxim*e on the results of 0.02 ppm HgCl2 exposure, 3 (33.3)%) isolates were still susceptible to *Cefotaxim*e and 6 (66.7%) isolates were resistant to *Cefotaxim*e. On the first day of exposure to *Cefotaxim* on the results of exposure to HgCl2 0.10 ppm, there were no (0%) isolates that were still susceptible to *Cefotaxim*e and 9 (100%) isolates that were resistant to *Cefotaxim*e. On the first day of exposure to *Cefotaxime* on the results of exposure to HgCl2 0.20 ppm, 2 (22.2)%) were still susceptible to *Cefotaxim*e and 7 (77.8%) isolates were resistant to *Cefotaxim*e.

This is consistent with research conducted by Ayu (2013) from the Biology Department, Faculty of Mathematics and Natural Sciences, Hasanuddin University, Makassar. In her research, the isolation of bacteria from seawater samples from Losari Beach was carried out using nutrient agar for Synthetic Seawater (NA ALS) media with added mercury at a concentration level of 0.02µg / ml. Then the bacterial isolates were tested for antibiotic resistance using antibiotic paper disks (Oxoid) including *Ampicillin* 10µg, *Novobiocyn* 30µg, *Chloramphenicol* 30µg, *Cefoperazone* 75µg, and *Ofloxacin* 5µg. Three types of isolates are resistant to mercury (Hg) and the antibiotics obtained are: mercury I resistant bacteria isolates which are also resistant to *Ofloxacin* 5µg, mercury resistant bacteria II isolates that are resistant to *Ampicillin* 10µg and mercury III resistant bacteria isolate that is resistant to all types of antibiotics.

In plasmids or transposons, it may also stimulate the formation of genes coding for resistance to several antibiotics, one of which is in the enzyme-producing bacteria ESBL, where ESBL is mostly derived from TEM and SHV enzymes, and in lesser amounts than CTX (Walker et al., 2015) where ESBL coding genes can be chromosomal or plasmidal. The resistance mechanism of each class of antibiotics can be different from other groups. Some researchers mention cross-resistance between different antibiotic classes (Canton and Coque, 2006; Talan et al., 2016). Changes in *E. coli* which are initially sensitive to non-ESBL mercury, but because living in an environment that has high mercury levels can changes it to ESBL mercury-resistant *E. coli* (Chojnacka, 2010)

Conclusion

The *E. coli* bacteria in the urine in sample body is mercury-resistant *E. coli*. This is proved by the results of exposure to mercury with concentrations of 0.02 ppm, 0.10 ppm, 0.20 ppm. It was found that all 30 samples of the study were mercury-resistant *E. coli*. Exposure to *Cefotaxime* for 1 day by invitro to mercury-resistant *E. coli* isolates non ESBL caused changes in 22 *E. coli* isolates in the urine. This proves that exposure to HgCl2 with various concentrations to *E. coli* isolates can accelerate the phenotic change from non-ESBL *E. coli* to ESBL *E. coli*.

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Characteristics of PPROM in General Hospital Dr. Soetomo Surabaya Period September 2017 to September 2019

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ABSTRACT

Background: Preterm Prelabour Rupture of Membranes (PPROM) is one of the causes of perinatal morbidity and mortality. **Objective:** To find out the characteristic of PPROM in Dr. Soetomo Hospital in September 2018 to September 2019**. Method:** A Retrospective Descriptive Study. The data came from the medical records of patients with PPROM who were included in the inclusion criteria. The exclusion criteria is all PPROM cases at Gestational age > 34 weeks. **Result:** The incidence of PPROM during September 2017 to September 2019 was 6.8% (175 patients), of which 152 patients included NBC cases and 23 patients with BC cases. Primipara 76 patients and Multipara 99 patients. For gestational age <26 weeks it was 17.1%, 26-30 weeks 29.7% and 31-34 weeks 53.1%. In this study, PPROM was amused 23.6%, underweight 3.1%, HBsAg 7.5%, HIV 7%, anemia 10.3%, Obesity 5.2%, Pragestational Diabetes 7.4%, Gestational Diabetes. 2,6%, preeclampsia 7,9% and severe preeclampsia 2,2%. The distribution of PPROM patients who received lung maturation was 72%, while the remaining 28% did not get lung maturation. Type of delivery for PPROM cases was vaginal delivery as much as 60% while 40% for cesarean section. Indications for vaginal delivery include fetal distress 25%, abnormal NST 18%, gemeli 17%, BSC 12%, febris 10%, pulmonary edema 5% and breech presentation 5%. The outcome distribution of PPROM infants born with asphyxia at birth was 87%. Weight of babies born with PPROM> 2500 g 4%, 1000-2500 g 73% and <1000 g 23%. The condition of the babies at birth with spontaneous breathing was 36 babies, nasal O2 was 13 babies and CPAP was 70 babies. The causes of death for preterm KPP babies included RDS 9 babies, Sepsis 4 babies and severe asphyxia 19 babies. The length of NICU care for infants who died with KPP Preterm mothers was <24 hours for 15 babies, 1-3 days 13 babies, 4-7 days 3 babies,> 7 days 3 babies and 5 fetuses were IUFD. 12 patients with PPROM received amnioinfusion while 5 patients with amniopatch, Outcome of infants from conservative PPROM who were treated with amniopatch or amnioinfusion obtained 6 babies died at birth, 8 babies with CPAP breath support, 1 baby with PCV breath support, 1 baby with ventilator and 1 infant spontaneously breathed. A total of 3 babies were outpatient after treatment for a maximum of ± 25 days. **Conclusion:** Perinatal care is currently experiencing some rapid progress, but the case of PPROM is still one of the biggest contributors to perinatal morbidity and mortality.

Introduction

Preterm Prelabour Rupture of Membranes (PPROM) is a rupture of the amniotic membrane at <37 weeks of gestation (Shailja, 2020). The incidence of PPROM occurs in 3-8% of pregnancies (Okeke, 2014) and in about 20% of the causes of preterm labor. This can lead to

significant perinatal morbidity. PPROM with gestational age less than 34 weeks can be considered to have a conservative therapy. Indication for PPROM's termination is at <34 weeks of gestational age. However, if there is an emergency in the fetus, chorioamnionitis, preterm in labor or when the gestational age can exceed >34 weeks. (Medina, 2006). There are 3 divided risk factor due to the etiology of the PPROM which are maternal risk factor (such as History of Previous PPROM, Anemia, BMI <20 kg/m2 nutritional deficiencies, low socioeconomic status, too young to get pregnant or U> 35 years, smoke, collagen vascular disorders (ex.SLE)), infant risk factor (such as multiple pregnancy anomalies (malformations, aneuploidies)) and uteroplacental risk factor (for example anomalies in the uterus (uterine septum), placental abruption, history of cervical conization, infection (ex: chorioamnionitis) (Cunningham, 2014).

Purpose

General Purpose

Describe the characteristics of pregnant patients who experience conservative PPROM (gestational age <34 weeks) in Dr. Soetomo Hospital for period September 2017 to September 2019.

Specific Purpose

Describes pregnant women with PPROM receiving conservative therapy and the output of infant from September 2017 to September 2019. Trying to find PPROM with gestational age <34 weeks under conservative therapy can reach until > 34 weeks of gestational age.

Benefit

Providing information about the characteristics of pregnancy with PPROM (<34 weeks of gestational age) to patients who visited during the period September 2017 to September 2019 at Dr. Soetomo Hospital in Surabaya

This research can be used as a reference to improve the quality of maternal services for the management of pregnancy with PPROM

Methods

A Retrospective Descriptive Study

- Using Delivery ward's register book, Medical Records and Morning Report's file for period September 2017 to September 2019

Inclusion Criteria

All cases of PPROM (<34 weeks of gestational age) that occurred at Dr. Soetomo Hospital in Surabaya from September 2017 to September 2019

Exclusion Criteria

All cases of PPROM at >34 weeks of gestational age.

Result

Table 1. Incidence of PPROM Dr. Soetomo Hospital in September 2017 to September 2019

Characteristic	Total	%
2018	93	3,6%
2019	82	3,2%

Table 2. Distribution of KPP Preterm patients at RSUD Dr. Soetomo based on the type of reference for the period September 2017 to September 2019

Referral Type	Total	%
NBC	152	86,9%
BC	23	13,1%

Table 3. Distribution of PPROM patients at Dr. Soetomo Hospital based on age from September 2017 to September 2019

Age	Total	%
Year 2018		
<20 th	9	1,5%
21-35 th	64	10,6%
>35 th	20	3,32%
Year 2019		

<20 th	11	2,11%
21-35 th	59	11,3%
>35 th	12	2,3%

Table 4. Distribution of PPROM patients at Dr. Soetomo Hospital based on parity for the period September 2017 to September 2019

Paritas	Total	%	Preterm Cases/2 years
Primipara	76	43%	9,28%
Multipara	99	57%	5,06%

Table 5. Distribution of PPROM patients at Dr. Soetomo Hospital based on the gestational age when rupture of membrane first occurred for the period September 2017 to September 2019

PPROM occur	Total	%
<26 week	30	17,1%
26-30 week	52	29,7%
31-34 week	93	53,1%

Table 6. Distribution of PPROM patients at RSUD Dr. Soetomo who received Lung Maturation from September 2017 to September 2019

Lung Maturation	Total	%
	126	72%

Table 7. Distribution of patients with PPROM Dr. Soetomo Hospital based on risk factors for PPROM from September 2017 to September 2019

Risk Factor	Total	% from preterm cases/2 years
Gemeli	17	23,6 %
Underweight	1	3,1%
HbsAg	6	7,5%
HIV	4	7%
Anemia	46	10,3%
Obesity	40	5,2%
Pragestasional Diabetes	4	7,4%
Gestasional Diabetes	2	2,6%
Preeklampsia	10	7,9%
Severe Preeklampsia	16	2,2%

Table 8. Distribution of PPROM patients at Dr. Soetomo Hospital who received Conservative treatment from September 2017 to September 2019

Conservative	Total	%
Amniopatch	5	26%
Amnioinfusi	14	74%

Table 9. Distribution of conservative PPROM patients with Amnioinfusion Dr. Soetomo in September 2017 to September 2019

No	Name	Parity	Gestational Age	Baby gender	Birth Weight	Apgar score	Breathing
1.	LIS	Primi	24/25 week	P	630 g	3-5	CPAP
2.	WIN	Primi	24/25 week	L	550 g	0	Died
3.	TIK	Gravida 2	26/27 week	L	800 g	1-3-5	Died
4.	SIH	Primi	27/28 week	L	1300 g	1-0	Died
5.	WAH	Gravida 2	24/25 week	L	600 g	3-5-7	CPAP
6.	PUT	Primi	23/24 week	L/L	540g /500g	1-0/0	Died
7.	LIS	Primi	28 week	L	950 g	1-1-3-5	PCV
8.	HIL	Primi	21/22 week	Hard to tio evaluate	500 g	1-1-0	
9.	RAF	Gravida 2	29/30 week	P	1200 g	5-6	CPAP
10.	DIA	Gravida 4	24/25 week	L	950 g	1-1-3	Ventilator
11.	RAK	Primi	31/32 week	P	1000 g	7-8	CPAP
12.	DEL	Gravida 3	30/31 week	P	1390 g	5-7	CPAP

Table 10. Distribution of conservative PPROM patients with Amniopatch Dr. Soetomo Hospital in September 2017 to September 2019

No	Name	Parity	Gestational Age	Baby Gender	Birth Weight	Apgar Score	Breathing
1.	EKA	Gravida 4	33/34 week	P	2000 g	5-6	Spontaneous
2.	DIP	Primi	27/28 week	P	1300 g	5-7	CPAP
3.	DEV	Primi	30/31 week	L	1500 g	6-7	CPAP
4.	TKW	Gravida 4	23/24 week	L	500 g	0	Died
5.	FIR	Gravida 3	30/31 week	L	1000 g	5-7	CPAP

Table 11. Distribution of Mode of Delivery for Patients with PPROM Dr. Soetomo Hospital in September 2017 to September 2019

Mode of Delivery	Total	%
Vaginal Delivery	92	61%
Cesarean Section	60	39%

Table 12. Distribution of Caesarean Section Indication in Patients with PPROM Dr. Soetomo Hospital in September 2017 to September 2019

CS Indication	Total	%
Fetal Distress	15	25 %
Abnormal NST	11	18 %
Gemeli	10	17 %
BSC	7	12 %
Fever	6	10 %
Breech presentation	3	5 %
Severe Preeclampsia & Lung Oedema	3	5 %
	5	8 %

Table 13. Baby Outcomes from PPROM at birth Dr. Soetomo in September 2017 to September 2019

Outcome baby	Total	%
Asfiksia (+)	90	87 %
Asfiksia (-)	14	13 %

Table 14. Distribution of baby outcomes from PPROM based on Birth Weight at Dr. Soetomo Hospital in September 2017 to September 2019

Birth Weight	Total	%
>2500 g	6	4 %
1000-2500 g	110	73 %
<1000 g	34	23 %

Table 15. Distribution on the Breathing Aid of PPROM's baby at birth in September 2017 to September 2019

Breathing Aid	Jumlah
Spontaneous	36
O2 nasal	13
CPAP	70
Ventilator	8
Death	38

Table 16. Distribution the causes of infant mortality in PPROM Patients in September 2017 to September 2019

Causes of death	total	%
IUFD	5	13 %
RDS	9	24 %
Sepsis	4	11 %
Low Birth Weight	1	3 %
Severe Asfiksia	19	50 %

Table 17. Distribution the length of day in NICU among infants who died Dr. Soetomo Hospital in September 2017 to September 2019

The Length of Day in NICU	Total	%
< 24 hours	14	37 %
1-3 Day	13	34 %
4-7 Day	3	8 %
>7 Day	3	8 %

Table 18. Distribution of Survival babies receiving Amniopatch / Amniosynthesis Treatment for PPROM in September 2017 to September 2019

No	Name	Gestational Age	Conservative Treatment	Birth Weight/ Apgar Score	Diagnosis	Length of Stay in NICU
1.	EKA	33/34 week	Amniopatch	2000g/AS 5-6	Bacterial Sepsis	7 hari
2.	DEV	33/34 week	Amniopatch	1500g/AS 5-7	BBLR, Bacterial Sepsis	22 hari
3.	DEL	30/31 week	Amnioinfusi	1390/AS 5-7	Anemia,Trombositopenia, BBLR	25 hari

Discussion

The sample in this study was dominated by mothers in reproductive age, mostly the age of 21-35 years from September 2017 to September 2019. The results of this study are in accordance with research conducted by Tengku et al which stated that the case of PPROM in Prof. Dr. R. D. Kandou Menado in 2018 mostly aged 20-35 years. This is supported by another study conducted in India by Mohan et al, which states that most cases are in the 20-30th age of mothers. (Mohan *et al.*, 2017)

The number of PPROM patients with gestational age <34 weeks from September 2017 to September 2019 were 175 patients, where NBC cases were 86.9% and BC cases were 13.1%. These results are consistent with the research conducted by Khade et al in India where Non Booked Cases were bigger than Booked Cases. This is due to inadequate Antenatal care which results in a lack of identification of risk factors in early pregnancy.

In the PPROM cases from September 2017 to September 2019, there were more patients with multiparous (99 patients) than mothers with primiparous (76 patients). The study conducted by Khade et al showed the same result, mostly multiparous (52%) were higher than primiparous (48%). The incidence of PPROM was found in many multiparous mothers because frequent pregnancies can affect embryogenesis so that the formed amniotic membrane will be thinner and prone to rupture, and amniotic infection is easier to occur due to damage to the cervical structure in previous deliveries. Distribution of PPROM patients with Gemeli pregnancy for the period of September 2017 to September 2019, there were 17 patients, which if calculated as a whole with the number of preterm deliveries, 23.6% of preterm deliveries were obtained. Whereas in the case of PPROM with underweight mothers, there was only 1 patient during a 2 year period. There were 6 patients with HBsAg and 4 patients with HIV. The results showed that a total of 7% of HIV patients with preterm KPP. This is consistent with a study conducted by Chidebere *et al* in KwaZulu-Natal, South Africa, which found that the incidence of preterm KPP was not high in patients with HIV (Chidebere, 2017).

PPROM before 26 weeks can delay lung development and can cause pulmonary hypoplasia (Van Teeffelen, 2014). Pulmonary hypoplasia is a term to describe an altered pulmonary development characterised by a reduction in the number of pulmonary alveoli or in bronchial branching. In fetal lung development a critical interval, the canalicular phase, exists between 16 and 28 weeks gestation. Gestational age at rupture of membranes has been shown to be inversely related to the risk of pulmonary hypoplasia. (Porat *et al.*, 2012). In this study, the distribution of PPROM patients who received lung maturation for preventing pulmonary hypoplasia was 72%, while the remaining 28% did not get lung maturation.

Type of delivery for PPROM cases was vaginal delivery as much as 60% while 40% for cesarean section. Indications for vaginal delivery include fetal distress 25%, abnormal NST 18%, gemeli 17%, BSC 12%, febris 10%, pulmonary edema 5% and breech presentation 5%. The outcome distribution of PPROM infants born with asphyxia at birth was 87%. Weight of babies born with PPROM> 2500 g 4%, 1000-2500 g 73% and <1000 g 23%. The condition of the babies at birth with spontaneous breathing was 36 babies, nasal O2 was 13 babies and CPAP was 70 babies. The causes of death for preterm KPP babies

included RDS 9 babies, Sepsis 4 babies and severe asphyxia 19 babies.

The length of NICU care for infants who died with KPP Preterm mothers was <24 hours for 15 babies, 1-3 days 13 babies, 4-7 days 3 babies,> 7 days 3 babies and 5 fetuses were IUFD. Amnioinfusion might improve fetal outcome by preventing pulmonary hypoplasia (Hofmeyr, 2014), by preventing neurological complications, increasing time to delivery interval, and improving fetal biophysical profile through prevention of umbilical cord compression. It also might prevent fetal deformity (Porat *et al.*, 2012). 12 patients with PPROM in this study received amnioinfusion while 5 patients with amniopatch, The outcome of infants from this conservative PPROM who were treated with amniopatch or amnioinfusion obtained 6 babies died at birth, 8 babies with CPAP breath support, 1 baby with PCV breath support, 1 baby with ventilator and 1 infant spontaneously breathed. A total of 3 babies were outpatient after treatment for a maximum of ± 25 days.

Conclusion

Premature infant puts immense burden on the economy and health care resources of the country. Therefore, management of PPROM requires accurate diagnosis and evaluation of the risk factors and benefits of continued pregnancy or expeditious delivery.

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The Use of Prophylactic Antibiotics on Orthopaedic Procedures in an Academic Hospital in Indonesia

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ABSTRACT

Background: Surgical site infections (SSIs) are common surgical complications that will increase cost of treatment. The incidence of SSI can be prevented with antibiotic prophylactic. Uncompliance using of prophylactic antibiotics is one of the factors leading to the occurrence a microbes resistance. The data on the using of prophylactic antibiotics in Indonesia is still limited. Objective: This study aims to analyze the using of prophylactic antibiotic guideline on orthopaedic surgery. Methods: The study was conducted retrospectively using data from medical records on patients who had clean and clean-contaminated orthopedic procedures from 2013 to 2016 in the standard operating room of Dr. Soetomo hospital Surabaya. We analyzed the use of prophylactic antibiotics in terms of antibiotic selection, timing of administration, and the compliance to the prophylactic antibiotic local guidelines on orthopaedic surgery. Results: Overall, patient data from 2013 to 2016 was 5246 patients. The compliance rate of prophylactic antibiotics from 2013 to 2016 was 48.3%. This level of compliance uses a selection of antibiotics, dose of administration, delivery mode, delivery time, and route of administration. Conclusion: The results of this study have shown that the prophylactic antibiotic compliance rate on orthophaedic procedures in Soetomo Hospital from 2013 to 2016 was 48,3%. Antibiotic resistance control program quite effective at increasing compliance with the use of the prophylaxis antibiotics.

Introduction

Surgical Site Infection (SSI) is a frequent infection in the surgical area of postoperative patients within 30 days of surgery or within a year after the implant surgery (Al-Mulhim *et al.*, 2014). Although standard prophylactic antibiotics have been used on surgical techniques, (SSI) case is still a serious complication of surgery.

In the United States, the incidence rate of SSI reached 1.07%, of which 8000 patients died from wound infections. US government also has spent over US$ 10bn on medical expenses (NHDS, 2010). UK should provide an additional fee of around £ 2500 to deal with SSI problems. The rough estimates indicate that the SSI increased the Long of Stay (LOS) for approximately 10 days and increased

additional costs up to US$ 2000 (NHDS, 2010). In Indonesia, the SSI case varies between 2-18% in all surgical procedures (Ong and Paraton, 2014). SSI problems in Dr. Soetomo hospital Surabaya ranged from 2-4% for clean wound operation and 5-15% for contaminated clean operation (Baktijasa *et al.*, 2014). The Surgical Site Infection (SSI) prevalence rate from PPI report of Dr Soetomo hospital in 2016 was 0.41% (Baktijasa *et al.*, 2014).

The overall methods to control infection case including improving correct hand washing campaign, operating room ventilation, sterilization methods, barriers, surgical techniques and the availability of prophylactic antibiotics. The Surgical Site Infection (SSI) remains the primary cause of morbidity, prolonged hospitalization, and increased mortality (Bratzler *et al.*, 2013). An infection mainly affects the implant surgery (orthopedic) operations patients (Mistry *et al.*, 2013). The complications common occur, particularly in the case of Surgical Site Infection (JP, 2012). The use of antimicrobials in orthopedic surgery is routinely used in prosthesis surgery either total-hip replacement (THR) or total-knee replacement (TKR), or surgery for implantation like nail, wire, plate, and screw (Mistry *et al.*, 2013). Nevertheless, the level of compliance with guidelines in the international scale ranged from 0 to 71.9%, while in Indonesia compliance with prophylactic antibiotic guidelines is limited (Syachroni, 2015).

The Surgical Site Infection more frequently happened among patient with immunodeficiency, diabetes mellitus, obesity, severe malnutrition and malignancy. SSI can be influenced by the factors including the use of prophylactic antibiotics, operating room ventilation, and surgery techniques (Tieman and Hofmann, 2009). In pre-operation, it includes skin preparation by not cleaning the surgical area or not shaving in the surgery area (Mistry *et al.*, 2013). The intra-operation factors a surgical technique must be done carefully to avoid excessive tissue damage, bleeding, infection, and drainage. The nutrition, personal hygiene, mobilization and wound care are the factors in the post-operation (Gagliardi *et al.*, 2009).

This study aims is to analyze the using of prophylactic antibiotic guideline orthopaedic surgery on clean and clean contaminated orthopedic procedure in 2013-2016 at Dr. Soetomo hospital Surabaya.

Methods

This research design was observational with retrospective study conducted in Dr. Soetomo hospital Surabaya. The orthopedic patients who underwent clean or clean contaminated surgery in the operating room of GBPT Dr. Soetomo hospital Surabaya were all included. Data were collected from patient's medical records from January 2013 until December 2016. The inclusion criteria were all orthopedic patients who underwent clean operation and or clean contamination at operating room RSUD Dr. Soetomo hospital Surabaya, from January 2013 to December 2016. The exclusion criteria were patients who had open fractures, multiple trauma, second surgery, history of open fractures, had preoperative infectious diseases at admission, an allergic history to all antibiotics, and received administration antibiotics more 24 hours before surgery.

We categorized the use of prophylactic antibiotics following the local guideline as the compliant group, while the non-

compliant group did not adhere to at least one of the following three criteria. Firstly, antibiotic selection for prophylactic treatment should entail intravenous cefazolin 1 gram (2 grams for a patient with an estimated body weight of 86 kg or more), or intravenous cefuroxime at 1.5 gram. If patients were intolerant to penicillin antibiotics, intravenous aminoglycosides were considered as alternative agents. Secondly, the prophylactic antibiotic should be administered between 30 and 60 minutes before the initial incision to achieve the optimal concentration in the incision area. Thirdly, the prophylactic antibiotic was used as a single dose. Repeated dosing could be allowed for surgical procedures with a prolonged operation (more than 4 hours) or a massive bleeding case (more than 1,500 ml). We analyzed the use of prophylactic antibiotics and devide it in the compliant group and non-compliant group.

In addition the collected *Case Report Form* (CRF) data, fieldwork researchers, who were firstly trained for conducting data collection and study management training, namely essential document training, manual procedure training, and data management training, were then filled them. The research stages covered the preparation, training for data collection team, conducting research, supervision, data analysis, editing, coding, processing, cleaning, and tabulation. The study has been approved by the ethical committee of Dr. Soetomo Hospital (No. 0654/KEPK/IX/2018).

Results

The study collected the data of 5246 patients: 3187 were male (61%) and 2059 were female (39%) (Picture 1).

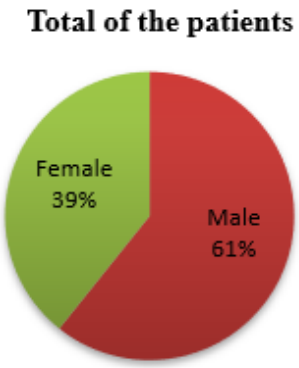

Figure 1. Pie Chart of Patient's Frequency

The age of groups are divided in 3 categories: < 20 years old, 20 – 60 years old and > 60 years old. The age distribution of the patients can be seen from the following table.

Table 1. Frequency Distribution of Patient Age Group

Age category	Total of the patients	
	Total	**Percentage (%)**
< 20	1201	22,9
20-60	3948	75,3
> 60	97	1,8
Total	**5246**	**100,0**

Table 1. informs that the patients in 20-60 years old group were the most dominant respondent, 3948 out of 5246. On the contrary, patients older than 60 years old group were 97.

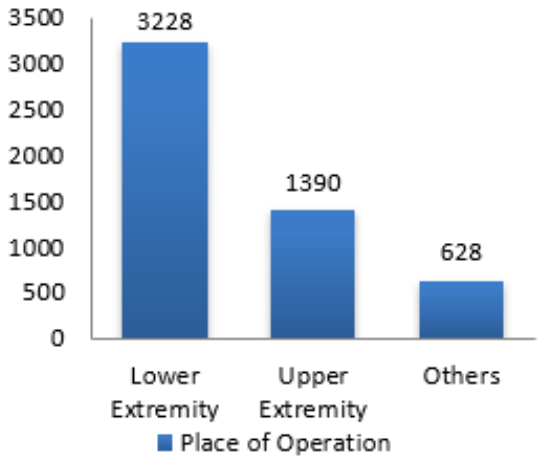

Figure 2. The Locations of Clean and Clean Contaminated Procedures

The most regio operation was *lower extremity* (3228 patients) followed by *upper extremity*, (1390 patients) (Picture 2).

Table 2. Frequency Distribution of Antibiotics

Type of antibiotics	Patient	
	Total	**Percentage (%)**
Cefazolin	4928	94,0
Ceftriaxone	318	6,0
Total	**5246**	**100,0**

Table 2. shows that cefazolin was the mostly used antibiotics, to 4928 patients. On the other hand, ceftriaxone was only given to 318 patients.

Table 3. Frequency Distribution Antibiotic Giving Time

Antibiotic giving time	Patient	
	Total	**Percentage (%)**
< 30 minutes	1936	36,9
30 - 60 minutes	2620	50,0
> 60 minutes	690	13,2
Total	5246	100,0

The prophylactic antibiotics were mostly given in 30-60 minutes (2620 patients, 50%).

Table 4. Level of antibiotic use compliance toward prophylaxis

Year	Compliant		Not compliant	
	Total	**Percentage (%)**	**Total**	**Percentage (%)**
2013	659	50,8	638	49,2
2014	688	51,6	646	48,4
2015	576	44,6	715	55,4
2016	610	46,1	714	53,9
Total 2013-2016	**2533**	**48,3**	**2713**	**51,7**

Based on table 4, we can infer that the level of antibiotic use compliance in 2013 was 50, 8%, 51,6% in 2014, 44,6% in 2015, and 46,1% in 2016. In total, the level of prophylactic antibiotic compliance from 2013 to 2016 was 48,3%.

Discussion

Several factors examined in this study were gender, age group, time of antibiotic administration, level of compliance to prophylactic antibiotics. The data demonstrated that the total of the patients were 3187 males (61%) and 2059 females (39%). This is likely related to most of the orthopedic surgeries caused by trauma or musculoskeletal injuries. The risk of trauma or musculoskeletal injuries in male might cause such percentage differences. It is correspondence with Tangarajah et al.'s examining open reduction internal fixation ankle complications (p= 0, 33) (Thangarajah *et al.,* 2009).

The infection mostly occured in the age of 32-40 years old. This result, however, was not significant using Chi Square (p= 0,845). The previous studies claimed that such infection case frequently occurs in > 60 years old group, for instance, reporting that there was a significant effect of post-operation infection in > 60 years old group, and Anderson's work notifying that there was a higher complication effect in > 60 years old group than others (Agodi *et al.,* 2015).

Prophylactic antibiotics in this study used 2 types of antibiotics, namely Cefazolin (4928 patients) and Ceftriaxon (318 patients). The level compliance of Cefazolin from 2013 to 2016 as a prophylactic antibiotic was 94%. Cefazolin is a first class cephalosporin antibiotic that is recommended for use as a prophylactic antibiotic in the field of orthopedics (Sanchez-Santana et al., 2017). Musmar (2014) found that the use of first generation cephalosporins as prophylactic antibiotics for clean surgery was 18.5% (Musmar et al., 2014). Nevertheless, Ong et all at Soetomo Hospital found that the

use of first-generation cephalosporins as antibiotic prophylaxis for clean surgery was 60.2% (Ong and Paraton, 2014). Meanwhile, Syachroni's study at hospital in Jakarta (2015), prophylactic antibiotics in clean and clean contaminated operations were Ceftriaxon as much as 49.8%. Ceftriaxon is a third generation cephalosporin (Syachroni, 2015).

According to Mistry et all (2013), first generation cephalosporins have high activity against Gram positive cocci (S. aureus) and moderate activity against Gram negative bacteria (E. Coli, Klebsiella), while second and third generation cephalosporins have higher activity in Gram negative compared to Gram positive bacteria Mistry *et al.,* 2013). Second and third generation cephalosporins are more expensive, their use increases the risk of resistance, especially against Gram negative rods. Therefore, the use of second or third generation cephaloporins as prophylactic antibiotics in orthopedics should be avoided.

The prophylactic antibiotics administration time before incision in this study, under 30 minutes was 36,9%, 30-60 minutes was 50% and over 60 minutes was 13,2%. Prophylactic antibiotics are mostly given within 60 minutes before the incision. According to Bratzler et al (2013), the optimal time for prophylactic antibiotics is 60 minutes before the incision begins. Some drugs, such as fluoroquinolone and vancomycin, need 1 to 2 hours of administration before the incision (Bratzler et al., 2013).

Hawn et al (2013) explained that the selection time for 60 minutes of prophylactic antibiotics was based on two points of evidence, antibiotic pharmacokinetics and one cohort study which analyzed the relationship between antibiotic administration and the incidence of SSI. The basic principle of prophylactic antibiotics in surgery is to achieve adequate serum and tissue drug levels during surgery (Musmar *et al.,* 2014).

Almost all guidelines recommended the use of SAP (Surgical Antimicrobial Prophylaxis) should be discontinued for less than 24 hours (Baktijasa et al., 2009). Previous research in Spain compared the use of single-dose Cefazolin (2 g) and 24-hour Cefazolin use (2 g initial dose, followed by 1 g every 8 hours) at heart surgery. The result was that SSI occurred twice more in the single-dose group (8.3% vs 3.6%, respectively, P = 0.004). However, most of the other studies comparing single-dose use to multiple doses have failed to show advantages in multiple-dose uses (Mannien *et al.,* 2006).

The compliance prophylactic antibiotic on orthopedic surgery in Soetomo Hospital between 2013-2016 was 48% among all procedures. Syachroni (2015) explains that the level of compliance to prophylactic antibiotics is associated with cultural factors, educational background, personal preferences, training, influence from institutions and drug supplies (Syachroni, 2015).

According to the ASHP, antibiotics for surgical prophylaxis should (1) prevent Surgical Wound Infection, (2) prevent Surgical Wound Infection-related morbidity and mortality, (3) reduce duration and health care costs, (4) no side effects, and (5) no have adverse consequences for the normal flora of the patient or hospital (ASHP, 2013). Cephalosporins, such as Cefazolin are first-line agents suitable for most surgical procedures, targeting organisms causing surgical wound infection by avoiding

broad-spectrum antimicrobial therapy that can lead to the development of antimicrobial resistance (Misrty *et al.*, 2013).

Sanchez et al.'s conducted a study on the effects of prophylactic antibiotic compliance which the results showed that adherence to antibiotic prophylaxis led into 4.2% of SSI cases. This lower occurrence indicates the administration of prophylactic antibiotics will reduce the SSI matter (Sanchez-Santana, 2107). The prophylactic antibiotic giving showed the efficacy to prevent and reduce the frequency of local infection surgery. In some study reports, the infection reduction of local surgery at the location of the operation reaches 56 % (Lin et al., 2104).

Conclusion

The results of this study have shown that the prophylactic antibiotic compliance rate on orthophaedic procedures in Soetomo Hospital from 2013 to 2016 was 48,3%. Antibiotic resistance control program quite effective at increasing compliance with the use of the prophylaxis antibiotics.

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