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Surface Contamination Of Covid-19: How Long Can The Virus Last?

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The novel coronavirus, which is now known as COVID-19, has caused a global pandemic. It is known that the main transmission routes of the novel coronavirus are through droplets, close human-to-human contact, and contact with inanimate surfaces contaminated by the virus. Thus, it is important to find out how long SARS-CoV-2 can remain viable on different surfaces. A study by van Doremalen et al. (2020) found that SARS-CoV-2 can remain viable for up to 72 hours on plastic and stainless steel surfaces, 4 hours on copper, and 24 hours on cardboard. Chin et al. (2020) reported that SARS-CoV-2 could persist on wood and cloth for 2 days, and could last for 4 days on glass and banknotes. These findings indicate that viral contamination of object surfaces is an important and dangerous factor in spread of disease, emphasizing the urgent need for prevention strategies against transmission of infection through contact with inanimate surfaces.

In December 2019, cases of pneumonia caused by the novel β-coronavirus first occurred in Wuhan, China, and went on to cause a global pandemic. On February 11th 2020, WHO officially named the new coronavirus disease as Coronavirus Disease 2019 (COVID-19).[1] The routes of transmission known are through droplets, direct human-to-human contact, and indirect contact via contaminated surfaces of inanimate objects.[2]

Indirect contact has become one of the most important contributors to disease spread, supported by findings from several studies. A study by Ong et al. (2020) has reported the presence of SARS-CoV-2 in samples from patients' rooms taken before routine cleaning, found especially on air outlet fans and the toilet area (sink, and door handles).[3] Ye et al. (2020) found that the virus could be found on various environmental surfaces throughout the hospital, commonly used hospital objects such as keyboards and doorknobs, medical equipments, and also personal protective equipments, mainly from hand sanitizer dispensers and gloves,[2] while another study have found an especially high positive rate of SARS-CoV-2 from floor swab samples.[4] A study by Chia et al. (2020) reported that the highest concentrations of SARS-CoV-2 in the air and on surfaces in a patient's environment are found during the first week of COVID-19 illness.[5]

Chin et al. (2020) found that the stability of SARS-CoV-2 varies on different types of surfaces and in varying environmental conditions, and is significantly affected by temperature.[6] The virus remained viable for 2 days on wood and cloth, while it could last longer, for up to 4 days, on glass and banknotes. SARS-CoV-2 is very stable in a temperature of 4^{o}C, with an estimated reduction of only 0,7 log unit of its infectious tire by the 14th day, while a temperature of 70^{o}C could shorten its inactivation time into only 5 minutes.[6]

A study by Doremalen et al. (2020) comparing the stability and rate of decay of SARS-CoV-2 and SARS-CoV-1 looked at five different media and environmental surfaces including aerosols, plastic, stainless steel, copper, and cardboard.[7] The results of this study revealed that SARS-CoV-2 could remain viable on plastic and stainless steel surfaces for 72 hours, on cardboard for 24 hours, on copper for 4 hours, and for 3 hours in aerosols.[7] On the other hand, although SARS-CoV-1 remained detectable in aerosols, on plastic, and on stainless steel for a similar duration, the results were different on cardboard and copper, which was 8 hours for both.[7] In comparison, MERS-CoV lasted for 48 hours on steel and on plastic.[8]

Although SARS-CoV-2 share some characteristics with SARS-CoV-1, they are not entirely the same. The same is true as with MERS-CoV. SARS-CoV-2 could remain viable for up to days on inanimate surfaces, highlighting the risk of transmission of the virus through this route.

The importance of through environmental cleaning cannot be underrated. Available evidence has shown that current decontamination measures performed in hospitals are sufficient.[3]

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Pilot Study for *Azoxymethane-induced Colon Cancer* in *Male Wistar Rats*

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Abstract

Introduction : The use of animal models could significantly further the elucidation of Colorectal Cancer (CRC) molecular pathogenesis and help in the discovery of preventive and therapeutic agents for the disease. Dimethylhydrazine (DMH) is a widely used chemical agent for Carcinogen induced CRC model. As agent, DMH is however becoming less readily available; hence in this Pilot Study we use Azoxymethane (AOM), a DMH metabolite as an alternative agent to induce CRC in male Wistar rats.

Methods: Forty two male Wistar rats at six weeks of age were randomly assigned into negative control groups and groups receiving two AOM injections subcutaneously (SC) within one week interval at 15 mg/kg body weight (BW) and 20 mg/kg BW respectively. Rats were sacrificed 8, 16 and 24 weeks post- AOM administration. Aberrant crypt foci (ACF) were analyzed. Tumor foci were characterized by gross examination and histopathological characteristics.

Results: All rats in the AOM groups developed tumors in the colonic mucosa. Formation of ACF was detected starting from 8 weeks post-AOM injection. The highest number of ACF with multiple crypts was observed at 16 weeks post-AOM administration. The total number of ACF did not vary between the two AOM doses. Mild, moderate and severe dysplastic cells were observed in colonic mucosa starting 8 weeks post-AOM injection. There was no statistically significant difference between number of severe dysplastic cells between the two AOM doses.

Conclusion: Administration of AOM 15 mg/kg BW SC is able to induce CRC in male Wistar rats. Higher dose is not necessary since it does not result in higher tumor incidence. This cancer model may be utilized to study chemopreventive effect of various agents in the future.

Introduction

Colorectal cancer is the second leading cause of cancer morbidity and mortality worldwide. Almost half of the world's population will develop at least one benign adenomatous colonic polyp in their lifetime, with less than 3% of those cases going on to develop colorectal cancer [1]. Almost 55% of the cases occur in developed countries. In Indonesia colorectal cancer is an emerging public disease health problem and currently among the three most prevalent types of cancer [2].

Research on colon cancer has benefited from the use of *in vitro* cell culture, and biopsy specimens. However, these methods have their own limitations. Colon cancer cell lines are able to grow *in vitro* without common micro environments such as interaction with matrix and stromal cell signal. In an *in vivo* setting however colon cancer cells rely on these factors for tissue homeostasis. Additionally, biopsy specimens taken from an individual may come from tumor which has developed over a long period and acquired complex mutational changes.
Therefore, their use may limit research on tumor initiation or promotion in which the genetic and environmental diversity should be controlled. Controlled *in vivo* studies in animal models are therefore considered as

important means to understand the molecular mechanisms of colorectal carcinogenesis for development of potential preventative and therapeutic strategies using a complex physiology of the colon [3, 4].

In order to maintain the translational potential of animal models for colon cancer, some characteristics are considered important. The cancer that develops in the animal model should be confined to the large intestine so that the development of the disease could be studied without confounding effects in other tissues. The histologic and molecular features should be similarly found in human colorectal cancer tissues. Additionally, the animal models should reflect the multifaceted intracellular pathways that are relevant to human colon cancer [3, 4].

Several colon cancer animal models have showed potentials for studying various initiating and environmental factors, specific dietary and genetic factors, as well as therapeutic options. These models can be categorized into induced and transgenic animal models, and each of these models differ in their relevance for studying various factors [3, 4]. Chemically or environmentally induced rodent model for colorectal cancer includes the administration of "Western diet", Heterocyclic amine, and alkylating agent such as N-methyl-N-nitro-N-nitrosoguanidine (MNNG) and N-methyl-N-nitrosourea (MNU) as well as 1,2-Dimethylhydrazine (DMH) or its metabolite Azoxymethane (AOM).

Each animal model offers its own advantages and disadvantages. The Western Diet model can be considered a good model for spontaneous colon cancer, but it requires a long period of induction and there is a lack of report on carcinogenesis steps in molecular level [5-6]. PhIP (2-amino-1-methyl-6-phenylimidozo [4,5-b] pyridine) is a heterocyclic amine byproduct from meat and fish cooking. In mice, PhIP induces formation of colonic aberrant crypt foci but not colon tumors. This model requires long period of induction with low tumor incidence rate [7-9]. MNNG and MNU are direct alkylating agents that induce colonic adenoma and carcinoma in a manner similar to histopathologic features of DMH induced model. Administration of both agents result in high incidence of colorectal cancer however these direct-acing carcinogens also induce neoplasia in organs other than colon, which turns into a confounding variable for this model [4].

DMH and its metabolite are most commonly used alkylating agents for sporadic CRC animal model. Repetitive treatment with this methylating agent was reported to produce colon tumors in rodents that exhibit many of the molecular and pathological features associated with the human sporadic CRC. In addition, this model offer advantages in term of cost, potency and convenience towards other chemical carcinogens [4, 10-14]. As a carcinogenic agent, DMH is becoming less readily available in Indonesia. This, in turn, requires that we search for comparable alternative. DMH metabolite, AOM, requires fewer metabolic activation step and is structurally closer to the ultimate carcinogen. Similar to DMH, AOM has been shown to promote histological and molecular changes that correspond with the orderly events' sequence that leads to the development of colorectal cancer. As the Wistar rats available at local vendors in Indonesia are not specific pathogen free animals, and with less defined genetic background, a pilot study is therefore necessary to investigate both AOM effect and appropriate dosage that will induce colon cancer in these animals.

Materials and Methods

Reagents

Azoxymethane, Hematoxylin, Eosin and Methylene blue were purchased from Sigma (St. Louis, MO, USA).

Animals

Forty-two adult male Wistar rats (100-120g) at six weeks of age were purchased from PT Indoanilab (Bogor, Indonesia). All rats were housed in conventional polypropylene plastic cages under controlled conditions (temperature of 25±2°C, humidity of 50±10%, and 12-hour light-dark cycles). The rats had free access to drinking water and were fed a basal diet containing 5% fat, 53% carbohydrate, and 25% protein (Laboratory Feed Industry, Bogor Agricultural University, Bogor, Indonesia). The rats were observed daily and their body weight was measured weekly.

CRC Induction

After three weeks acclimatization period (BW 120-150 g), the rats were randomly assigned into nine groups. Group 1, 4 and 7 served as negative control groups. Rats in these groups received saline treatment and were sacrificed at week 9, 17 and 25 respectively. Group 2, 5, and 8 were given two injections of AOM dissolved in normal saline, at 15 mg/kg BW subcutaneously within 1-week interval. Rats in these groups were sacrificed at week 9, 17 and 25 (8, 16 and 24 weeks after last AOM administration) respectively. Groups 3, 6 and 9 received two injections of AOM dissolved in normal saline, at 20 mg/kg BW subcutaneously; and were sacrificed at week 9, 17 and 25 (8, 16 and 24 weeks after last AOM administration). Euthanasia was performed by injection of Ketamine and Xylazine using three times the dose of Ketamine-Xylazine for anesthesia [15]. All studies were performed with the approval of the research ethics review committee of Mochtar Riady Institute for Nanotechnology (No. 001/MRIN-EX/ECL/I/2017).

Aberrant Crypt Foci (ACF) Identification

For ACF Analysis, we followed protocol as reported in Lu et al. [16]. Rats' colons were removed, rinsed in ice-cold 1X PBS pH 7.4, slit open longitudinally, and fixed flat between two filter papers which have been soaked in PBS. The colons were incubated in 10% neutral buffered formalin for 18 hours and subsequently stained with 0.2% methylene blue for 10 seconds. Methylene blue solution were prepared using the same formalin solution. Deeply stained crypts were inspected after staining, and the total number of ACF and the number of aberrant crypts (ACs) in each focus were counted under a light microscope at 100X magnification (Axioskop 40, Zeiss, Germany).

Histological Assay

All rats were examined grossly at necropsy. The intestine from the stomach to anus were removed and the large intestine were isolated.

The large intestine was slit open lengthwise, washed in saline and the mucosal surface was examined for gross pathology. Any lesions detected were measured, their location noted and the lesions were dissected. Normal appearing colons and a portion of the lesions were taken for histological examination, after fixation in 10% w/v formaldehyde overnight according to standard methods. After fixation, the lesions were embedded in paraffin, sectioned at 4 µm, stained with Hematoxylin and Eosin for evaluation under a light microscope at 10X and 40X Magnification (Axioskop 40, Zeiss, Germany).

Calculation of tumor incidence, number and volume

The tumor incidence, average tumor number and tumor size were calculated using formula as described by Jia et al. [17]. Tumor incidence calculated from the number of rats that developed tumors in the colon tissue after twice injection of AOM during the experiment.

Characterization and Calculation of dysplastic cells

Histopathological classification was based on criteria as described in [18]. In brief mild, moderate and severe dysplasia were categorized by the form of nuclei, cell polarity, structure of glandular epithelium, and the presence of goblet cells and immune cells in the mucosal layer. The presence of dysplastic cells was carefully noted in terms of classification, and number along 3 separate sections covering 10 areas of the colon tumor.

Statistical Analysis

For statistical analysis, values are expressed as means ± SD. All statistics were computed using SPSS21 (SPSS Software, SPSS Inc., Chicago, USA). Unpaired Student's t test and chi-square test were used to detect statistically significant differences between groups. A P-value of < 0.05 is considered significant.

Result

Physical parameters

The time course of the experiment and the animal treatment procedures are shown in Figure 1. Over the six-month period, all rats showed an increase in body weight. No significant difference in bodyweight gain was observed between the groups. Fig. 2 illustrates the body weight development during the entire duration of the experiment. Following AOM injections, the body weight of rats in both AOM groups was significantly lower compared to the control groups. At the end of 8 weeks, rats receiving AOM at 15 mg/kg BW and 20 mg/kg BW showed a decrease in body weight compared to rats in control groups (One-way ANOVA, P = 8E-3). At the end of 8 weeks after AOM injection, the mean body weight for control groups was 212.39±11.47 g, for AOM dose 15 mg/kg BW it was 184.08±10.61 g (post-hoc analysis, P = 0.077), and for rats receiving AOM 20 mg/kg BW the mean body weight was 155.61±8.01 g (post-hoc analysis, P=0.002). Similarly, at the end of 24 weeks, rats in AOM groups showed a lower bodyweight than control rats (One-way ANOVA, P = 0.0013). The mean body weight at the end of 24 weeks for control groups was 260.66±4.09 g, it decreased to 236.59±4.34 g for AOM dose 15 mg/kg BW (post-hoc analysis, P = 0.0012), and it further decreased to 222.84±15.28 g for rats receiving AOM 20 mg/kg BW (post-hoc analysis, P=0.0139). The body weight of rats in groups receiving AOM on average was lower than rats in control groups at the end of 16 weeks, however it was not statistically significant.

Tumor Incidence

Tumors were visualized in general by gross examination in colon tissue at the end of the experiment. Multiple nodules were detected macroscopically in the colonic mucosa of rats induced with both AOM doses with diameter ranging from 3 mm to 1.5 cm. The number of nodules in colonic mucosa of rats in the AOM groups are listed in Table 1.
Tumor incidence is determined by calculating the percentage of tumor-bearing rats from total rats in the group. Tumor-bearing rats are the number of rats with tumors developed in the colonic mucosa with the repeated injection of AOM during the whole experiment process. In this Pilot Study, both AOM doses resulted in 100% tumor incidence, as all rats treated with AOM developed tumor in the colonic mucosa in the course of the experiment. There was a statistically significant increase of mean tumor volume with longer induction period at AOM 15 mg/ kg BW. The mean tumor volume at 8 weeks post-AOM injection was 18.4±4.70 which increased to 35.45±10.46 mm^3 at 16 weeks and to 83.3±10.98 mm^3 at 24 weeks after the second AOM injection. No significant difference in tumor number and tumor volume was observed with longer induction period at AOM 20 mg/ kg BW. Figure 3 shows nodules detected in the colonic tissues of rats in AOM groups. Few nodules in colonic mucosa were detected in some rats in control groups. However, upon further observation, the nodules were identified as infiltrating lymphocyte to mucosal layer, and no dysplastic cells were detected (data not shown).

Aberrant Crypt Foci (ACF)

ACF are considered as potential pre-neoplastic lesions of the colon in both humans and experimental animals. ACF were distinguished from surrounding normal crypts by increased size, thickened epithelial cell lining, and enlarged cryptal area relative to surrounding normal crypts. Figure 4 shows normal cell colon and colon containing foci with 2, 3 and more than 4 aberrant crypts in rats treated with AOM.

Table 2 illustrates total number of ACF and number of foci that was detected in rats from all groups. ACF is further categorized by the number of aberrant crypts (1, 2, 3 or more than 4) formed in the foci. There was a significant difference in the number of ACF between 8 weeks and 16 weeks or 24 weeks experiment time (Fig.5A and B). In rats receiving two injections of AOM at 15 mg/kg BW, mean number of ACF after 8 weeks was 9.40±3.40, the number increased significantly to 31.60±2.16 after 16 weeks (P = 5E-4) and to 33.40±4.65 foci 24 weeks after AOM induction (P = 0.0031). Similarly, in rats receiving two injections of AOM at 20 mg/kg BW, 8 weeks after induction the mean number of ACF was 11.00±2.89, this number increased significantly to 30.40±5.12(P = 0.0109) and to 36.28±4.42 (P = 0.0033) at 16 weeks and 24 weeks post-AOM induction, respectively. However, within the same induction time, there was no statistically significant difference in the mean ACF number between the two AOM doses (Fig.5A and B).

Histology Evaluation

For further confirmation of the presence of dysplastic cells, Hematoxylin and Eosin staining were performed. In control animals, colon crypts were detected with goblet cells and normal colonocytes (Fig 6 A and B). Normal histopathological structure of the mucosal layer with glandular structure, an underlying sub-mucosa and muscular layer were observed in the tissue section of the animals. In rats treated with AOM, proliferation of colonocytes and decrease of glandular architecture of the crypts were observed indicating the presence of dysplastic cells. Mild dysplasia was detected with proliferation of lymphoid and glandular structure in the mucosa layer (Fig. 6C and 6D). Additionally, moderate dysplasia was identified with lymphoid proliferation in mucosal layer and degeneration of the glandular lining epithelium with loss of nuclei (Fig. 6E and 6F). Tissue section with severe dysplasia showed abnormal hyperplastic glandular in mucosa layer, degeneration of epithelial with loss nuclei and proliferation lymphoid in mucosa layer were detected (Fig. 6G and 6H). Moreover, inflammatory cell infiltration in the lamina propria of the mucosal layer with intact mucosal epithelium was also detected (Fig. 7)

Fig. 8 illustrates the mean number of mild, moderate and severe dysplastic cells in both AOM doses at various induction time. There was no statistically significant difference between mean number of dysplastic cells in various induction time in animals receiving AOM 15 mg/kg BW. At AOM dose 15 mg/kg BW, mean number of mild, moderate and severe dysplastic cells did not differ significantly at 8 weeks, 16 weeks and 24 weeks after AOM induction (Fig. 7A, $P > 0.05$). At AOM dose 20 mg/ kg BW, mean number of mild dysplastic cells increased from 31±0.707 at 8 weeks to 33±0.316 at 16 weeks after AOM induction ($P = 0.0325$). Similarly, the longer the induction period, the greater was the number of cells which was categorized as severe dysplastic. At 8 weeks after AOM induction, the mean number of cells was 27±1.048; this number increased to 30.4±0.979 ($P = 0.045$) and to 32±2.049 ($P = 0.073$) at 16 weeks and 24 weeks respectively.

Discussion

In this Pilot Study, we use Azoxymethane (AOM), a DMH metabolite as an alternative agent to induce CRC in male Wistar rats. Similar to DMH, AOM has been shown to induce colon cancer in a manner comparable to the pathogenesis of human sporadic colon cancer. After administration, AOM is metabolised into Methylazoxymethanol (MAM) by CYP2E1, which generates DNA mutations. Mutations associated with colon carcinogenesis have been reported in DMH/ AOM cancer model, for instance mutations in K-ras and β-catenin. As a result of these mutations, associated PI3K/Akt and MAPK pathways are activated, and β-catenin degradation is prevented which leads to cell proliferation. In addition, Transforming Growth Factor Beta (TGFβ), a protein that is essential for apoptosis, has been shown to be inactivated in AOM cancer model [19]. Despite the safety aspects associated with the use of carcinogens, and the considerable time required for tumour development, DMH or AOM induced CRC animal model is considered useful for the study of the molecular biology, prevention and treatment of colon cancer [20].

In this study, 42 male Wistar rats nine weeks of age were distributed into control, and two AOM groups. Animals in AOM groups received two subcutaneous injections of AOM dissolved in saline at 15 mg/kg BW or 20 mg/ kg BW within one week period. Animals in control groups received the equivalent volume of saline with the same frequency as animals in AOM groups. In general, treatment with both AOM doses resulted in lower body weight compared to control in all time point. As no significant difference between the groups was observed in food intake, the low body weight in AOM group rats is mainly due to the increased tumour burden.

Tumor induction using AOM in rodents were genetically dependent. Compared to Fischer F-344 rats, Wistar rats showed greater percentage of colorectal tumors, and the distribution of tumors in colorectum resembled more the distribution found in human pathology in DMH model [23]. In our Pilot Study, both AOM doses resulted in 100% tumor incidence in Wistar rats at 8, 16 and 24 weeks after AOM administration, similar to reported in [24]. Aberrant Crypt Foci (ACF) were one of the first observed biomarkers for murine CRC model. ACF in humans have been characterized for altered enzymatic activity, crypt dynamics and

proliferation; and they were found to closely resemble aberrant crypts seen in rodents treated with carcinogens [21]. In our experiment, treatment with both AOM doses induced formation of ACF, and we observed a considerable increase of total ACF in rats 16 weeks post-AOM injection compared to 8 weeks. ACF with multiple crypts (≥4) were considered more prone to progress into cancer, and were suggested to be better predictors for tumor incidence [22]. ACF ≥4 crypts were detected in our study. There was a statistically significant difference in number of ACF ≥4 crypts at 16 weeks and 24 weeks in comparison to 8 weeks after AOM administration. However, similar ACF number and ACF types were detected in rats 16 weeks and 24 weeks post-AOM treatment between the two AOM doses, suggesting that the formation of ACF in our experiment was not in a dose-dependent manner.

Histopathologic classification was based on the following criteria. Mild dysplasia was characterized as having elongated, crowded and pseudo-stratified nuclei with preserved polarity and a normal or slightly reduced number of goblet cells. Moderate dysplasia was characterized as having hyperchromatic proprieties and deformity of the cell nuclei, increased number of mitoses, thickening of the glandular epithelium and an increased number of immune (defence) cells in the connective tissue. Severe dysplasia was characterized as having broad, round or ovoid nuclei with prominent nucleoli, and atypical mitotic figures. In severe dysplasia, the nuclear polarity was partially lost and the number of goblet cells was significantly reduced or completely disappeared [18]. In this Pilot Study, colon of rats in control group showed predominantly normal crypts in which goblet cells and normal glandular structure were present. AOM administration in both 15 mg/ kg BW and 20 mg/ kg BW doses resulted in the formation of mild, moderate and severe dysplastic cells starting from 8 weeks after last AOM injection. While number of severe dysplastic cells increased with longer period of induction at AOM 20 mg/ kg BW, there was no statistically significant difference between mean number of dysplastic cells in various induction time in animals receiving AOM 15 mg/kg BW.

In conclusion, administration of AOM as low as 15 mg/kg BW SC is able to induce colon carcinogenesis in male Wistar rats. Higher dose is not necessary since it does not result in higher tumor incidence. The development of colon carcinogenesis in the AOM rat model involves the formation of ACF lesion, mild, moderate and severe dysplastic cells which starts at 8 weeks and peaks at 16 weeks after AOM administration. Results of this pilot study can pave the way for further studies on the elucidation of Colorectal Cancer (CRC) molecular pathogenesis and the discovery of preventive and therapeutic agents for the disease.

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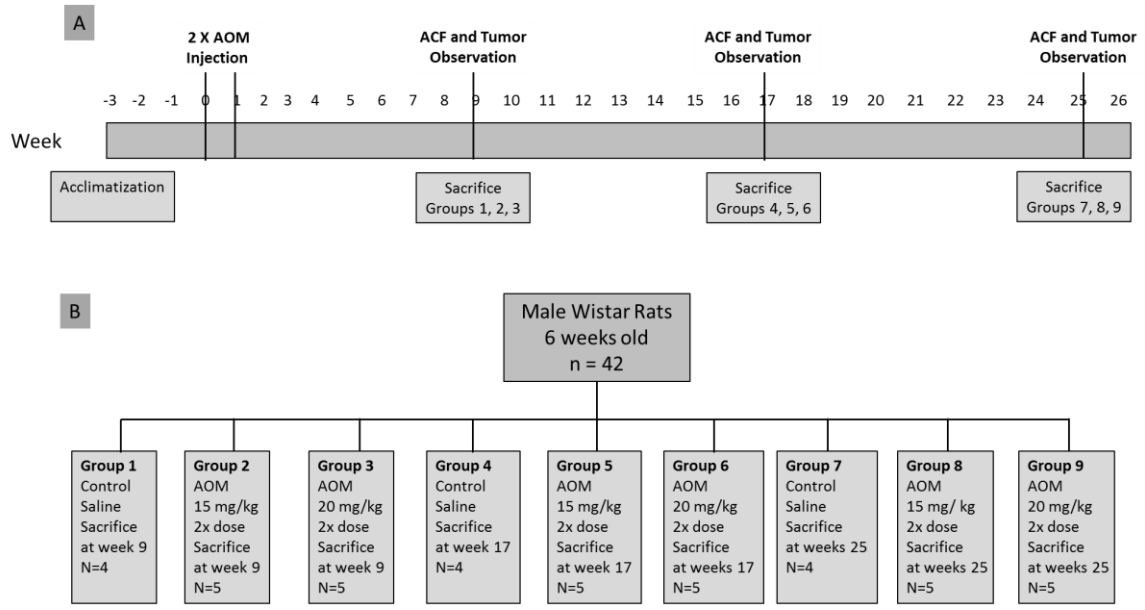

Fig.1. **Experimental Outline.** A. Timeline for AOM administration and sacrifice. B. Experimental group distribution. AOM was administered subcutaneously. AOM: Azoxymethane; ACF: Aberrant Crypt Foci

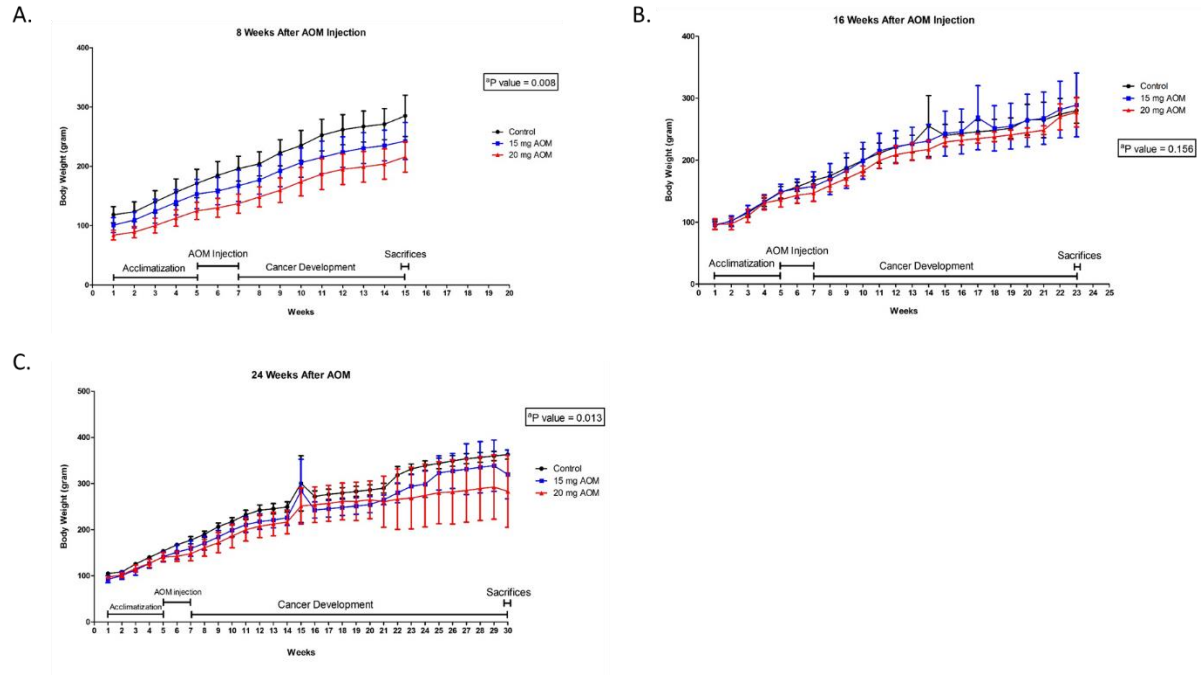

Fig.2. **Body weight development of rats in control and AOM treated groups.** A. 8 weeks- B. 16 weeks- C. 24 weeks- post AOM injection. Statistical Analysis using One-way ANOVA, $P < 0.05$ is considered significant.

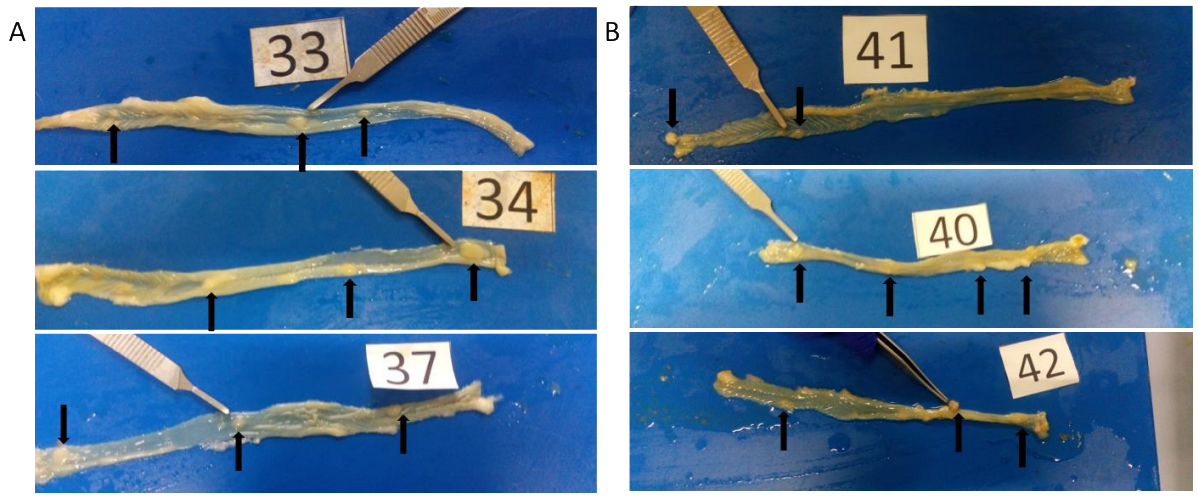

Fig.3. Nodules in colon of rats in AOM groups. Arrows indicate the presence of mucosal nodule A. 24 weeks after 2x injection of AOM 15 mg/kg BW B.24 weeks after 2X injection of AOM 20 mg/kg BW

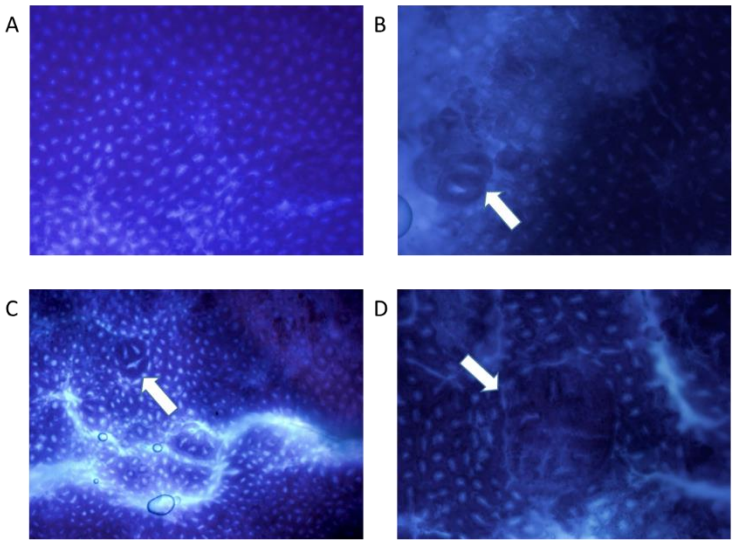

Fig.4. **ACF formation in control and AOM-induced animals.** A. Control group; Foci containing B. 2 aberrant crypts: C. 3 aberrant crypts: D. more than 4 aberrant crypts in rat treated with AOM 15 mg/ kg BW 16 weeks after AOM induction

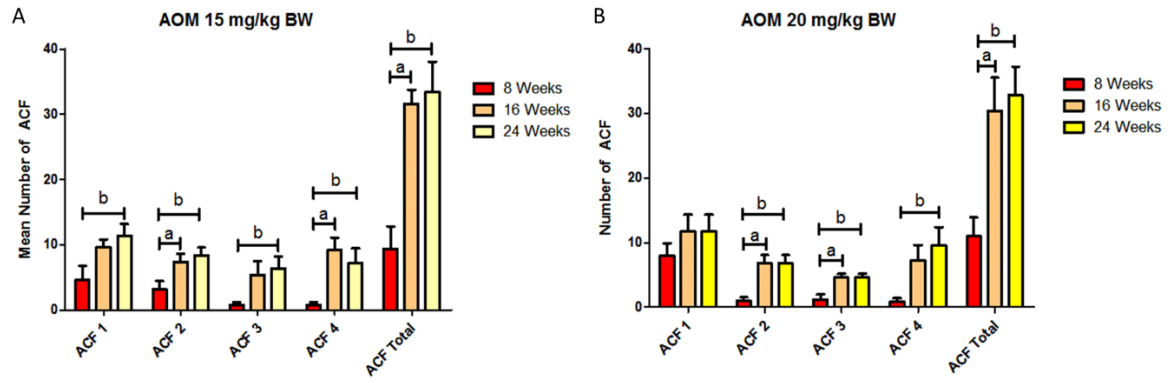

Fig.5. Total and average **number and type of ACF in AOM-induced animals.** A. 15 mg/kg BW. B. 20 mg/kg BW. Statistical analysis: a. t-test, $P < 0.05$, 8 weeks vs 16 weeks, b. t-test, $P < 0.05$, 8 weeks vs 24 weeks

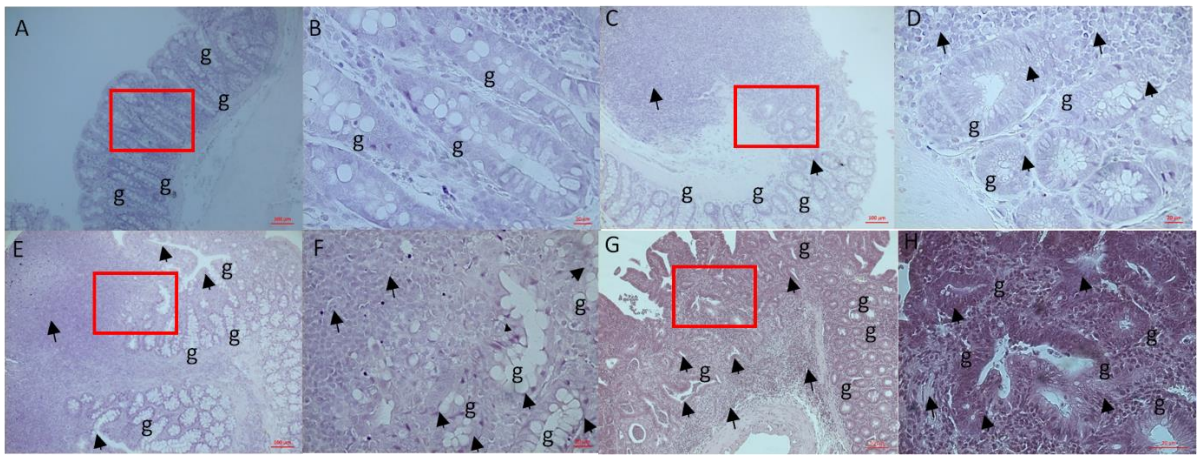

Fig. 6. Representative section of colon architecture histology under the light microscope after haematoxylin and eosin staining. A, B: Normal crypt of rat colon observed in control group. g = glandular structure. C, D: Mild dysplastic cells observed in rat's colon after induction with AOM 20 mg/kg BW. Arrows indicate lymphoid proliferation in mucosal layer. Arrowheads show proliferation of glandular structure in the mucosa layer. E, F: Moderate dysplasia. Arrows show lymphoid proliferation in mucosal layer. Arrowheads indicate degeneration of the glandular lining epithelium with loss of nuclei. G, H: Severe dysplasia observed in rat's colonic mucosa after treatment with AOM 15mg/kg BW; Arrows indicate lymphoid proliferation in mucosa layer; Arrowheads show proliferation glandular structure with loss of nuclei. (A, C, E, and G: 10X Magnification; B, D, F, and H: 40X Magnification)

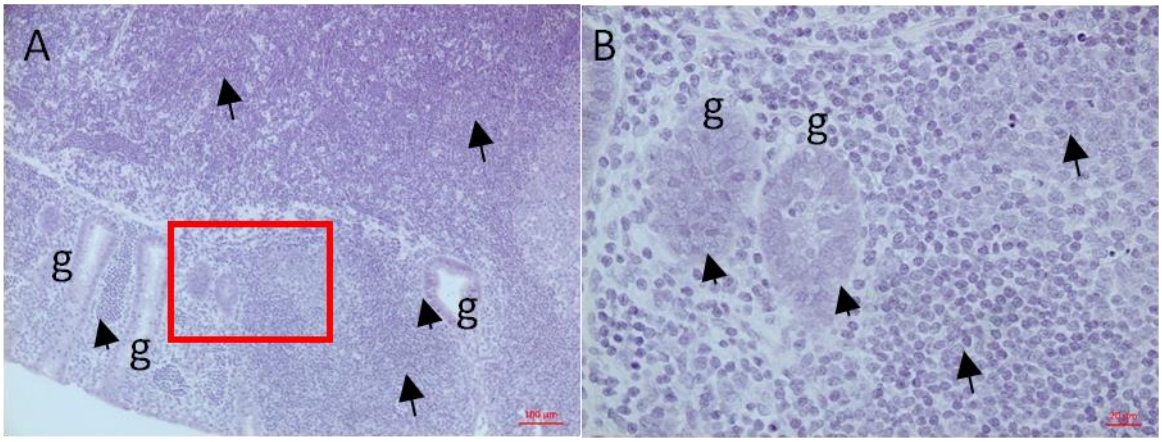

Fig. 7. Moderate dysplasia with inflammatory cell infiltration in the the mucosal layer. Arrow: lymphocyte cells. Arrowheads: glandular proliferation. A: 10X, B: 40X Magnification

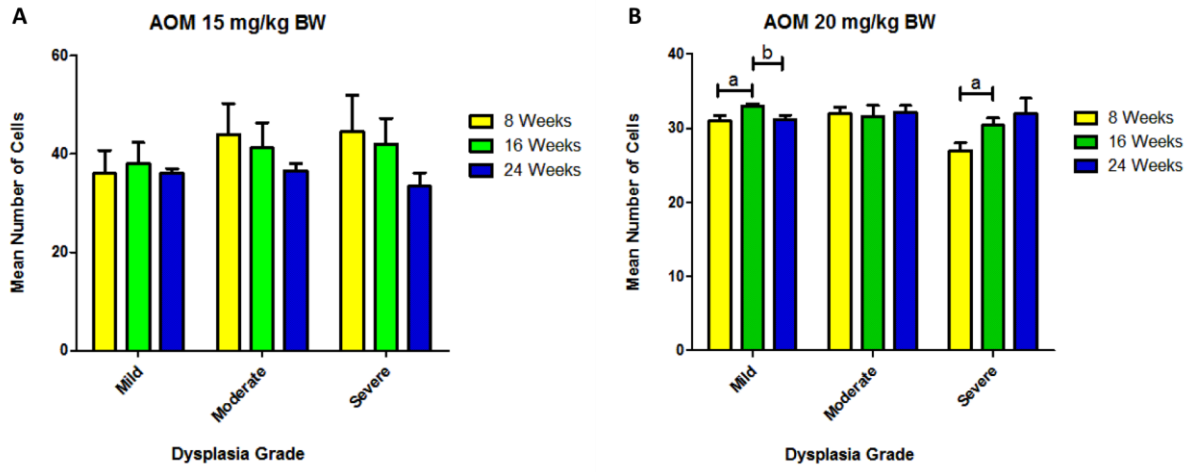

Fig. 8. Mean number of cells with different Dysplasia grade in rats induced with (A) AOM 15 mg/kg BW and (B) 20 mg/kg BW. Statistical analysis: a. t-test, $P < 0.05$, 8 weeks vs 16 weeks, b. t-test, $P < 0.05$, 16 weeks vs 24 weeks. There was no statistically significant difference between mean number of dysplastic cells in various induction time in animals receiving AOM 15 mg/kg BW.

Table 1. Incidence, number and volume of tumors

	Group					
AOM dose	15 mg/ kg BW			20 mg/ kg BW		
	8 wks	16 wks	24 wks	8 wks	16 wks	24 wks
n	5	5	5	5	5	5
Tumor-bearing rats	5	5	5	5	5	5
Tumor incidence	100%	100%	100%	100%	100%	100%
Number of tumors	18	12	21	18	19	16
Average tumor number	3.6 ± 0.75	2.4 ± 0.75	4.2 ± 0.66	3.6 ± 0.75	3.8 ± 0.66	3.2 ± 0.49
Tumor Volume (mm^3)	18.4±4.70	35.45±10.46	83.3±10.98[a,b]	64.3±14.00	72.4±13.89	45.3±6.89

Values are expressed as mean ±SEM. Average tumor number and tumor volume were analyzed using unpaired student's T-test. [a] *P* = 6E-4 (8wks vs 24 wks); [b]1*P* = 0.013 (16 wks vs 24 wks)

Table 2. AOM-induced ACF in rats' colon

Group	**n**	**total number of ACF/ rat**	**Number of foci containing**			
			1 crypt	2 crypts	3 crypt	≥4 crypts
Control 8 wks	4	0	0	0	0	0
Control 16 wks	4	0	0	0	0	0
Control 24 wks	4	0	0	0	0	0
AOM 15 mg/kg BW 8 wks	5	9.40±3.40	4.60±2.18	3.20±1.24	0.80±0.37	0.80±0.37
AOM 15 mg/kg BW 16 wks	5	31.60±2.16	9.60±1.20	7.40±1.24	5.40±2.11	9.20±1.93
AOM 15 mg/kg BW 24 wks	5	33.40±4.65	11.40±1.80	8.40±1.60	6.40±1.77	7.20±2.22
AOM 20 mg/kg BW 8 wks	5	11.00±2.89	8.00±1.92	1.00±0.54	1.20±0.80	0.80±0.58
AOM 20 mg/kg BW 16 wks	5	30.40±5.12	9.60±1.02	6.20±1.01	4.40±0.40	7.50±3.12
AOM 20 mg/kg BW 24 wks	5	36.28±4.42	11.80±2.51	6.80±1.28	4.60±0.60	9.60±2.80

Values are expressed as mean±SEM. Average ACF and aberrant crypts number were analyzed using unpaired student's T-test

Risk Factors of Cervical Cancer in Outpatient and Inpatient at Obstetric and Gynecology RSUP Dr. Mohammad Hoesin Palembang

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Abstract

Introduction: Cervical cancer is a malignant tumor originating from primary squamous epithelial cells and it is one of the several types of cancers that affects more to women.

Methods: This research uses descriptive analytic with case- control. The sample was 52 patients who divided into 26 patients with cervical cancer and 26 patients with non - cervical cancer were outpatient and inpatient at Department of Obstetrics and Gynecology Hospital Dr. Mohammad Hoesin Palembang during the period September 2016 -November 2016. This study uses primary data in the form of interviews. Data was analyzed by univariate and presented in a frequency distribution table. Furthermore, using bivariate analysis to determine the relationship and OR.

Result: From 8 risk factors studied, there is sygnificancy correlation between pathological vaginal discharge (p= 0,0005 OR= ∞), parity (p= 0,0005 OR= 22,7), age (p= 0,0005 OR= 19,2), oral contraception usage for a long time (p= 0,0005, OR= 12,4), age of the first intercourse (p= 0,006, OR= 6,1), and the husband's occupation (p= 0,05 OR= 3,6) with the incidence of cervical cancer. While, there are two risk factors that don't have a sygnificancy correlation between smoking (p= 1,0) and changing sexual partners (p= 1,0) with the incidence of cervical cancer.

Conclusion: The results of this research identified risk factors that significantly related to cervical cancer incidence was the age, the age of first sexual intercourse, parity, long-term oral contraceptive use, a history of vaginal discharge, and the husband's occupation.

Introduction

Cervical cancer is a primary cervical cancer originating from epithelial metaplasia in the columnar squamous junction region (SSK) which is a transitional area of the vaginal mucosa and cervical canal mucosa, where it is the second most common type of cancer affecting women worldwide, usually affecting women aged 35 -55 years.1 There are 270,000 women in the world every year diagnosed with cervical cancer and 85% are in developing countries including Indonesia 2 Cervical cancer is always followed by the HPV virus which is transmitted through sexual contact. It starts with precancerous lesions which after years can develop to be invasive. Although the main cause of cervical cancer is HPV infection, there are major risk factors for cervical cancer that can affect HPV infection, namely: Age, age of early sexual intercourse, smoking, high parity, long-term use of birth control pills, multiple sexual partners , vaginal discharge, and husband's work. These risk factors are very closely related to the occurrence of cervical cancer.

This research was conducted because Indonesia is the country with the first rank of cervical cancer. Palembang has a prevalence of 52% for the incidence of cervical cancer as evidenced by medical record data at RSUP Dr. Mohammad Hoesin Palembang where there were 657 cervical cancer events in 2015. In addition, data from the Ministry of Health showed that the risk factors outlined are the most important risk factors and play an important role in cervical cancer events. Therefore, a study was conducted on the risk factors for cervical cancer incidence in the polyclinic and inpatient obstetrics and gynecology departments of RSUP Dr. Mohammad Hoesin Palembang to know and examine more deeply about the risk factors that play an important role in increasing the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang, such as age, age at first sexual intercourse, parity, smoking, long-term use of oral contraceptives, changing sexual relations, history of vaginal discharge, and husband's work.

Methods

This research uses descriptive analytic research with case-control. Sampling of research using consecutive sampling techniques. The study sample was 52 patients who were divided into 26 cervical cancer patients as a case group and 26 non-cervical cancer patients as a control group both outpatient and inpatient at the Department of Obstetrics and Gynecology Dr. RSUP. Mohammad Hoesin Palembang during the period September-November 2016. This study uses primary data in the form of interviews. Data were analyzed univariately and presented in the form of a frequency distribution table. Next, it is analyzed bivariately to determine the relationship and OR values.

Result

Table 1 shows the distribution of patients based on sociodemographic characteristics consisting of residence, education level, and occupation. Of the 26 most cervical cancer patients (61.5%) who reside in Palembang, elementary school level (53.8%), and housewife occupation (76.9%). Of the 26 most non-cervical cancer patients (73.1%) residing in Palembang, high school education (53.8%), and housewife occupation (80.8%). The distribution of patients based on sociodemographic characteristics in the cervical and non-cervical cancer groups can be seen in table 1.

Table 2 shows the relationship and magnitude of risk factors for cervical cancer, with the results: There is a relationship between the age of the patient with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang, aged> 35 years, has a risk of developing cervical cancer 19.2 times greater than patients aged 20-35 years.

There is a relationship between the age of first sexual intercourse in patients with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang, who married at the age of under or equal to 20 years, had a risk of cervical cancer 6.1 times greater than patients who were married at the age of> 20 years.
There is a relationship between parity in patients with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang who has ≥ 3 children at risk of cervical cancer is 22.7 times greater than patients who have <3 children.

There is no relationship between smoking in patients with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang who smoked the risk of cervical cancer 0 times greater than patients who did not smoke.

There is a relationship between long-term use of oral contraceptives in patients with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang who used birth control pills> 4 years at risk of developing cervical cancer was 12.4 times greater than patients who were ≤ 4 years old or did not use birth control pills.

There is no relationship between changing sexual partners of research subjects with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang who has> 1 sexual partner is at risk of getting cervical cancer 0 times greater than patients who have 1 sexual partner.

There is a relationship between the history of pathological vaginal discharge in patients with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang who has a history of positive pathological vaginal discharge is at an increased risk of getting cervical cancer infinitely greater than patients who have a history of negative pathological vaginal discharge.

There is a relationship between the husband's work in patients with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang. Outpatients and inpatients at RSUP Dr. Mohammad Hoesin Palembang whose husband's work is often out of town at risk of getting cervical cancer 3.6 times greater than patients whose husband's work is not out of town.

Discussion

Relationship and Magnitude of Risk between Age and Cervical Cancer Occurrence

In this study of 52 patients, case group was> 35 years old (46.2%). Based on Chi-Square statistical tests, age> 35 years increases the risk of cervical cancer 19.2 times compared to those aged 20-35 years. The mean age of cervical cancer patients is between the ages of 30-70 years, where stage IA cervical cancer is more commonly found in the 30-39 years age group, while for stage II it is more often found in the 40-49 years age group, and the 60- 69 years is the highest proportion in stages III and IV[4]. Age is an important factor in cancer, most cancers occur in old age. The risk of cervical cancer has doubled after the age of 35 to 60 years[5] The association of age> 35 years with the incidence of cervical cancer is due to the time of exposure to HPV infection which is prolonged and the immune system is weakening due to thymus involution in old age. Those two things that cause age> 35 years have the potential to cause cervical cancer.

Relationship and Magnitude of Risk between the Age of First Sexual Relations with Cervical Cancer Occurrence

In this study of 52 patients, the case group with first age had sexual intercourse ≤ 20 years (36.5%). Based on the Chi-Square statistical test, the age of first sexual intercourse ≤ 20 years increases the risk of cervical cancer 6.1 times compared to the age of first sexual intercourse> 20 years. Age at first sexual intercourse is a risk factor for cervical cancer with a 2.54 times greater risk of having cervical cancer in women who have sexual intercourse ≤ 20 years compared to having sexual intercourse at age> 20 years.[6] Women who start sexual intercourse at a young age will increase their risk of cervical cancer, because cervical columnar cells are more sensitive to metaplasia during adulthood. then women who have sex before the age of 18-20 years will be at risk of cervical cancer 5 times greater[7]

The first link between sexual intercourse for ≤20 years with cervical cancer is that the cervix in adolescents is more susceptible to carcinogenic stimuli due to the process of squamous metaplasia being active in the transformation zone during the development period coupled with the entry of foreign substances such as sperm that can trigger changes cells become cancer cells. That is what causes the age of the first sexual intercourse ≤20 years has the potential to cause cervical cancer.

Relationship and Magnitude of Risk between Parity and Cervical Cancer Occurrence

In this study of 52 patients, case group with parity ≥ 3 (46.2%). Based on the Chi-Square statistical test, parity ≥ 3 children increased the risk of cervical cancer by 22.7 times greater than parity <3. Parity is a risk factor for cervical cancer with a 3 times greater risk of developing cervical cancer in women with parity ≥ 3 compared to women with parity <3.[8] The process of childbirth has a trauma effect or even the effect of decreasing body immunity thereby increasing the risk of HPV infection, where women who have 3 children are 4 times more likely to develop cervical cancer.[9] The linkage of parity ≥ 3 to the incidence of cervical cancer is due to hormonal changes, where very high progesterone during pregnancy can induce HPV oncogens. In addition, there is also a decrease in the immune system due to tolerance of the baby's semi-allogenic tissue which causes an increase in HPV transmission, plus again with injury to the birth canal that makes it easy to get infected with HPV at the time of delivery.

The Relationship and Magnitude of Risk between Smoking and Cervical Cancer Occurrence

In this study of 52 patients, the case group was smoking (48.1%). Based on the Chi-Square statistical test, there is no relationship between smoking and cervical cancer. Women who smoke are twice as likely to develop cervical cancer as those who do not smoke. This is because tobacco in cigarettes also contains carcinogenic substances (which cause cancer) both smoked as cigarettes and chewed cigarettes. This study does not have respondents who become active smokers because in social life, especially in Indonesia rarely women who smoke, so it does not affect[10]

Therefore, smoking actually influences the occurrence of cervical cancer but in this study there was no correlation between smoking and the incidence of cervical cancer because only a few women in Palembang smoked. That is what causes no link between smoking and cervical cancer.

Relationship and Magnitude of Risk between Long-term Use of Oral Contraception with Cervical Cancer Occurrence

In this study out of 52 patients, the case group used oral contraceptives> 4 years (34.6%). Based on Chi-Square statistical tests, it is known that long-term use of oral contraceptives> 4 years increases the risk of cervical cancer by 12.4 times compared to ≤4 years or not using birth control pills. oral contraceptives that are used for a longer period of more than 4 years can increase the risk of cervical cancer by 4 times. birth control pills contain estrogen and progesterone, both of which play a role in inducing HPV11 oncogens. Oral contraceptives in the form of birth control pills used for more than 4 years increase 1-1.5 times the risk of cervical cancer. That's because oral contraceptive pills consist of two artificial hormones that are the same as estrogen and progesterone. Consumption of birth control pills is more routine and prolonged, allowing women to suffer from cervical cancer[10]

Therefore, the association between> 4 years of oral contraceptive use and the incidence of cervical cancer due to the presence of the hormones estrogen and progesterone which play a role in increasing the growth of abnormal cells in the cervix and activating HPV oncogens so that there is an increase in cervical cancer progressivity.
That is why the use of oral contraceptives> 4 years has the potential to cause cervical cancer.

The Relationship and Magnitude of Risk between Changing Sexual Couples with Cervical Cancer Occurrence

In this study of 52 patients, a case group with> 1 sexual partner (0%). Based on Chi-Square statistical tests, there is no relationship between multiple sexual partners with the incidence of cervical cancer. A history of sexual intercourse of more than 1 person has a risk of 5 times greater for cervical cancer than those who do not, because there is a specific protein that is owned by every man. The protein has the property of causing damage to cervical epithelial cells, generally cervical epithelial cells will tolerate and recognize the protein. However, in women who have sexual intercourse> 1 man causes many sperm with different specific proteins that will cause damage without repair of cervical cells and potentially cause cervical cancer[7]

In this study only a few respondents claimed to have> 1 sexual partner in which respondents' dishonesty factor played a role in this regard.[10] The relationship between multiple sexual partners actually influences the occurrence of cervical cancer but in this study there was no relationship of changing sexual partners with the incidence of cervical cancer in which dishonesty factors were involved in this study. That is what causes no link between changing sexual partners with cervical cancer.

Relationship and Magnitude of Risk between Pathological Leucorrhoea History with Cervical Cancer Occurrence

In this study out of 52 patients, the case group experienced a pathological vaginal discharge (50%). Based on the Chi-Square statistical test, a pathological history of vaginal discharge increases the risk of cervical cancer by ∞ (infinite) times compared to those without a pathological vaginal discharge. A pathological history of vaginal discharge can increase the risk of cervical cancer by 4.9 times[5] Women who have a history of pathological vaginal discharge will be at risk of suffering from cervical cancer because Lactobacillus acidophlus plays an important role in

maintaining the vaginal environment by producing hydrogen peroxide which can make vaginal pH become low (acidic) which is 3.8-4.5. At this PH, pathogenic and viral bacteria can be easily killed so as to avoid genital infection.[12] The association of pathological vaginal discharge with cervical cancer due to a history of genital infection that inhibits Lactobacillus acidophilus to produce hydrogen peroxide so HPV can easily enter the cervix. That is what causes a history of pathological vaginal discharge that has the potential to cause cervical cancer

Relationship and Magnitude of Risk between husband's work with cervical cancer

In this study of 52 patients, the case group whose husband's work was often out of town (30.8%). Based on the Chi-Square statistical test, the husband's work that is often out of town increases the risk of cervical cancer by 3.6 times than that of her husband's work not out of town.

The work of a husband who is often out of town has a major effect on the occurrence of cervical cancer. Work A husband who is often out of town has little time to meet his wife, making it possible to have sexual relations with a female sex worker who often carries the HPV virus.[13] Many respondents who suffer from cervical cancer are those whose husbands work outside the city as many as 14.8% [14]

The linkage of the husband's work is often out of town with the occurrence of cervical cancer that is, due to rarely meeting his wife so they have sexual relations with sex workers who are vulnerable to transmit HPV. That is what causes the husband's work often out of town has the potential to cause cervical cancer

Conclusion

The Results of research on risk factors for cervical cancer in outpatients and inpatients at the Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang, it can be concluded:

1. There is a relationship of age with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang, aged> 35 years, is at risk of cervical cancer 19.2 times compared to patients aged 20 - 35 years.
2. There is a relationship between age at first sexual intercourse with cervical cancer at RSUP Dr. Mohammad Hoesin Palembang who had sexual intercourse for the first time ≤ 20 years at risk of cervical cancer 6.1 times than patients who had first sexual intercourse> 20 years.
3. There is a relationship between parity and the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang whose parity ≥ 3 is at risk of cervical cancer 22.7 times compared to patients whose parity <3.
4. There is no relationship between smoking and the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang.
5. There is a relationship between long-term use of oral contraceptives with the incidence of cervical cancer in RSUP Dr. Mohammad Hoesin Palembang who used birth control pills> 4 years had a risk of cervical cancer 12.4 times compared to patients who were ≤ 4 years old or did not use birth control pills.
6. There is no relationship of changing sexual partners with cervical cancer at RSUP Dr. Mohammad Hoesin Palembang.
7. There is a relationship between the history of pathological vaginal discharge in RSUP Dr. Mohammad Hoesin Palembang who has a history of positive pathological vaginal discharge has an infinite risk of cervical cancer than patients who have a history of negative pathological vaginal discharge.
8. There is a relationship between husband's work at RSUP Dr. Mohammad Hoesin Palembang whose husband's work is often out of town at risk of cervical cancer 3.6 times than in patients whose husband's work is not out of town

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Table 1. Characteristic Respondents

Variable cancer	Category	cervical cancer		Non cervical	
		n	%	n	%
Residence	Bangka Belitung	5	19,2	1	3,8
	Bengkulu	1	3,8	0	0,0
	Indralaya	0	0,0	3	11,5
	Jambi	1	3,8	1	3,8
	Lahat	1	3,8	0	0,0
	Muaraenim	0	0,0	1	3,8
	Palembang	16	61,5	19	73,1
	Prabumulih	0	0,0	1	3,8
	Tanjungenim	2	7,7	0	0,0
Education Level	Tidak Sekolah	2	7,7	2	7,7
	SD	14	53,8	2	7,7
	SLTP	2	7,7	3	11,5
	SLTA	7	26,9	14	53,8
	Tamat Akademi	1	3,8	5	19,2
Occupation	Bidan	1	3,8	0	0,0
	Guru	0	0,0	2	7,7
	Ibu Rumah Tangga	20	76,9	21	80,8
	Petani	4	15,4	1	3,8
	Pns	1	3,8	0	0,0
	Wiraswasta	0	0,0	2	7,7

Table 2. Relationship between Risk Factors and Cervical Cancer Occurrences (N=52)

Risk Factor	Cervical cancer		Non-Cervical cancer		*p*; OR
			n	%	
History of pathological vaginal discharge					
Negative	0	0,0	17	32,7	*0,0005*;*
Positive	26	50,0	9	17,3	*∞***
Parity					
<3 children	2	3,8	17	32,7	*0,0005;*
≥ 3 children	24	46,2	9	17,3	*22,7*
Age					
20 – 35 years old	2	3,8	16	30,8	*0,0005;*
> 35 years old	24	46,2	10	19,2	*19,2*
The use of long term contraceptives					
≤ 4 years or not using family planning pills	8	15,4	22	42,3	*0,0005;*
> 4 year using family planning pills	18	34,6	4	7,7	*12,4*
Age for the first time sexual intercourse					
≤20 years old	19	36,5	8	15,4	*0,006; 6,1*
>20 years old	7	13,5	18	34,6	
Husband's occupation					
Tidak ke luar kota	10	19,2	18	34,6	*0,05;*
Sering ke luar kota	16	30,8	8	15,4	*3,6*
Smoking					
Yes	1	1,9	0	0,0	*1,0*;*
No	25	48,1	26	50,0	*0*
Changing sexual partner					
1 Sexual partner	26	50,0	25	48,1	*1,0*;*
	0	0,0	1	1,9	*0*
>1 Sexual partners					

Note: Chi-Square

*Fisher Exact Test

Service Condition of Customer Service Inhealth Admision RSUP Dr. Mohammad Hoesin Palembang when Serves BPJS Patient in 2014

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Abstract

Introduction : Health Service includes administrative service. In RSUP Dr. Mohammad Hoesin Palembang, it is implemented by Customer Service Inhealth Admision. To describe the service condition of Customer Service Inhealth Admision when serves BPJS patients in 2014 based on the quality of service which are reliability, responsiveness, emphaty, tangible, and assurance and how it actualized them, it is necessary in depth interview and observation in Customer Service Inhealth Admision RSUP Dr. Mohammad Hoesin Palembang.
Method : This study used observation and in depth interview with respondents, which were chosen purposively. The data were then transcribed and analysed for themes using deductive content analysis.
Result : Service condition of Customer Service Inhealth Admision RSUP Dr. Mohammad Hoesin Palembang in 2014 is the service condition which are reliable and responsive, making efforts to actualize emphaty, tangible, and assurance aspects when serves the patients either BPJS or general before they hospitalized in RSUP Dr. Mohammad Hoesin Palembang.
Conclusion : Customer Service Inhealth Admision requires improvement, in particular the queue system for the patients who want to find their bed before they hospitalized. Employee of Customer Service Inhealth Admision should enhance their efforts to actualize emphaty and assurance aspects when serve the patients.

Introduction

One referral level, health care coverage is a continuation administration services include administrative costs of registration of participants for treatment, issuance eligibilities participants, including card making pasien 1.[1] At this level, at the Dr. Mohammad Hoesin Palembang Hospital, the process is carried out in the Admission Outpatient and Inpatient Admission.[2]

Customer Service Inpatient Admissions under Installation Public Relations, Marketing, and Customer Complaints duties are to not give information and education to patients and families.[3] In addition, Customer Service Inpatient Admissions has an important role for patients BPJS and patients who will undergo general inpatient beds, namely finding the appropriate class of disease and treatment of patients who will undergo hospitalization.[4]

The object
ives of this research were to see how the conditions of service in the Customer Service Admission Inpatient Hospital Dr. Mohammad Hoesin Palembang in serving patients BPJS 2014 in accordance with the five dimensions of service quality include reliability, responsiveness, empathy, tangible, and assurance2 and to know how to Customer Service Admission Inpatient Hospital Dr. Mohammad Hoesin Palembang in implementing the five dimensions of service according to the service quality, it is necessary to do in-depth interviews and observations at the Customer Service Admission Inpatient Dr. Mohammad Hoesin Hospital Palembang.

Method

This study was a qualitative study. Data was obtained through the observation in the study site and in-depth interviews to Key Informant sampling.[3]

This study was conducted in Customer Service Admission Inpatient Hospital Dr. Mohammad Hoesin Palembang in October-November 2014. The objectives of this research are to see how the conditions of service in the Customer Service Admission Inpatient Hospital Dr. Mohammad Hoesin Palembang in serving patients BPJS 2014 in accordance with the five dimensions of service quality include reliability, responsiveness, empathy, tangible, and assurance and to know how to Customer Service Admission Inpatient Hospital Dr. Mohammad Hoesin Palembang in implementing the five dimensions of service according to the service quality, it is necessary to do in-depth interviews and observations at the Customer Service Admission Inpatient Dr. Mohammad Hoesin Hospital Palembang.

Key Informant in this study consisted of five people from two different parties, namely the providers of care and use of services. Service providers in question is Customer Service Admission Inpatient Hospital Dr. Mohammad Hoesin Palembang, while users of services in question is the patient participants BPJS Health Class I, II, and III which will be hospitalized at the Hospital Dr. Mohammad Hoesin Palembang. Methods of collecting information from key informant using in-depth interviews. Long depth interviews varied between 6-76 minutes with a frequency of one-time interview. Characteristics of key informant consists of role and gender which is descried in Table 1.

The results of in-depth interviews and observations conducted transcription is then processed to qualitatively analyzed using deductive techniques analysis 4 content. In the analysis of the content of this deductive approach, the analysis starts from the things that are common toward the things that are special. Analyses were performed by encoding (coding) of data that are grouped into categories that have been made previously by the guidelines depth interviews in this study.

Result

1. Coordinator of Public Relations, Marketing, and Customer Complaints

Installation Complaints Marketing and Customer Relations is the container of public relations and marketing. It not only as a public relations public relations, but also him as a marketer. Marketing is inclusive of promotion, publicity, and customer complaints. Receive any complaints in internal or external. Marketing, that market products in RSMH, services, both of which featured, in the form of tools and services professionals.

2. Customer Service of Inpatient Admission

Based decision of director Dr. Mohammad Hoesin Palembang Number: KP.04.04/II/062/2014 are set out on January 6, 2014 that in order to improve the quality of service that is integrated in the Hospital Dr. Mohammad Hoesin Palembang, it is necessary to designated customer service officers in the department Dr. Mohammad Hoesin Palembang. The one who is responsibile is Installation of Public Relations, Marketing, and Customer Complaints. Customer Service Actually there are two, namely Customer Service Admission Outpatient and Inpatient Admission Customer Service. Specials Customer Service Inpatient Admissions that serve patients who will undergo hospitalization which is under the responsibility of Installation of Public Relations, Marketing, and Customer Complaints.

3. Function and Role of Customer Service of Inpatient Admission

The function and role of Customer Service Inpatient Admission is delivering general information. General information is thorough and general information that also still exist in quotes because there are limits given general information about it, including: the rights and obligations of patients, tat orderly, tariff, facilities space, privacy, and limits the number of visitors. In addition to providing general information, Customer Service Inpatient Admissions also find bed patient to be treated. Patients undergoing inpatient treatment will bring a letter from the clinic. From a letter of the care, Customer Service Inpatient Admissions will see how the guarantee in class. Thereafter, Customer Service Inpatient Admissions will find the beds of patients undergoing inpatient accordance with illness and guarantee in class.

4. Service Schedule of Customer Service of Inpatient Admission

The following is the interview results on the schedule of health service:

Key Informant 2: “Morning and noon, 2 shifts, 7.30 a.m–02.00 p.m and 02.00 p.m–09.00 p.m. Outside the shift, we have night workers from 09.00 p.m–07.30 a.m.”
Key Informant 3: “At 02.00 p.m we are already allowed to go home.”

The following is observation results from service department:
The schedule of Inpatient Admisiion Customer Service : Open 24 hours:
Morning: 08.00 a.m–02.00 p.m
Noon: 02.00 p.m–09.00 p.m
Evening: 09.00 p.m–08.00 a.

5. Length of Que to Obtain Inpatient Bed per day

To know the lenghth of que in one day, the observer questioned key informant 2, which answered: “3 hours. More than 3 hours, we advice them to go home.”

In additon, the observer also ask key informant 3, whcih gave the anser,”From morning until 02.00 a.m. After 02.00 p.m we allowed asked to go home.”

After that, the researchers conducted direct observation and found that on October 14, 2014 at 2:50 pm, no name calling patients who have been waiting to get a room, patients are called, patients are encouraged to go home and come back tomorrow to wait for up to 02.00 pm, room still full for all classes and disease. Fifteen patients were called.

6. Speed of Customer Care Inpatient Admission After Finding Patient’s Hospitalization Room

Here are the results of in-depth interview about the speed of service Customer Service Admission Inpatient after Getting Patients Hospitalization Room Confirmation:
Key Informant 2: “After obtaining room confirmation, we give general infirmation. The patient’s nameis inputted to the computer. Then the patient is given a medical record before admitted to the related room.”
Key Informant 4: “Only 10 minutes.”

From observation, we obtained:
Patient were given general infoirmation and then sign general consent (5-7 minutes)
Patient’s identity is inputted in computer and then medical record will be published (2-3 minutes).

7. Easiness to Obtain Care in Inpatient Admission Customer Service

The following is the result of interview on easiness to obtain care in inpatient admission customer service.
Key Informant 3: “When we arrived, we receive service directly.”
Key Informant 2: “If there were questions, we response to it rapidly.”

8. Justice of Officer Customer Service Inpatient Admissions in Providing Care To Patients

The following is te result of interview on justice of officer customer service inpatient admissions in providing care to patients:
Key Informant 2: “We give service equally. No corruption is allowed.”
Key Informant 4: “There are times when patient wants to pay even after we tried to explain that the room is full.”
Key Informant 3: “There were people that was last to come but obtain room earlier than the ones that has already queued.”
Key Informant 2: “Patients sometimes doesn’t understand that different diseases belongs to different room although under the same department.”

Based on observation results on 15th October 2014 at 08.10 a.m there was a patient that intended to express his/her complain to Customer Service Inpatient Admissions in Providing Care to Patients. The patient said that he/she has waited for a room for two days. The treatment he/she was supposed to undergo in two days. However, because of all the rooms were still occupied, the patients were still adviced to que.

9. Procedure after Obtaining Confirmation on Hospitalization Room

The following is the result of deep interview on procedure after obtaining confirmation on hospitalization room,
Key Informant 2: “After obtaining room confirmation, we give general infirmation. The patient’s name is inputted to the computer. Then the patient is given a medical record before admitted to the related room.”
Key Informant 3: “After being called, we were given general information and asked to sign some forms.”
Key Informat 4: “We fill in forms. Ten minutes is rewuired.”
Key Informant 5: “We just fill in forms.”

Based on observation that were obtained at 08.45 a.m on 15 th October 2014, the procedure after the patient obtain confirmation on hospitalization room are as the following:
1. The patient and/or relatives of patients who get an empty room in accordance with the disease and its treatment classes are called by the clerk Customer Service Inpatient to inform that empty room awaited already available and ready to be hospitalized.
2. The patient that has been called will be given general information
3. After given general information, the patient will sign a form of general information.
4. Patient will be given a paient card after his/her data is inputed into the computer.
5. After inputting patient's data, the patient will be given a medical record

10. Customer Service Officer of Inpatient Admission Giving Opportunities To Patients To Ask

The following is the result of interview on customer service officer inpatient admission giving opportunities to patients to ask
Key Informant 2: "We ask the patient to recall the information we had just given."
Key Informant 3: "We ask the patient whether they understand the information or not."
Key Informant 5: "We only ask about the disease and how many times we have to control."

11. Customer Service Officer Inpatient Admission In Responding to Patient's complain

The following is the result of interview on customer service officer inpatient admission in responding to patient's complain:
Key Informant 2: "We help patient with any difficulties that they encounter. We have provided a worker to assist patient if there were difficulties."
Key Informant 3: "We never complain. We just follow what we are told because we are afraid the administration will slow us down."

Based on observation, the Customer Service Officer of Inpatient Admission gave an answer when the patient asked, "What is the solution? I have been waiting for two days to book a room." The answer was, "We apologize for the incovenience. We really hope for your patience bcause all rooms are full."

12. Concern of Customer Service Officer of Inpatient Admission In Serving Patients

The following is the result of deep interview on the concern of customer service officer inpatient addmission in serving patient:
Key informant 2: "We are really concern about the patients. If the patient cannot read, we already have a worker that will assist tthe patient."
Key informant 3: "There was a good worker that will help us and really care for us."

13. Completeness of Infrastructures in Customer Service Inpatient Admission

The following is the result of deep interview on the completeness of infrastructure in Customer Service Inpatient Admission:
Key informant 1: "There are two television monitors, furnitures, and other facilities."
Key informant 3: "There are a lot of air conditioners, seats, and monitors. We don't have to stand for a long time and can follow up the availabilities of room through the monitor."

From observation, it is obtained that the facilities consists of seven air conditioners, one fan, two television monitor, and 104 seats The purpose of television monitor is to give information of vacant and occupied patient room.

14. The Leisure of Infrastructure in Customer Service Inpatient Admission

The following is the result of deep interview on the leisure of infrastructure of customer service inpatient admission:
Key informant 3: "The waiting room is already complete."
Key informant 1: "The condition of the room depends on the human resources."

15. The Cleanliness of Inpatient Admission Waiting Room

The following is the result of deep interview of the cleanliness of inpatient admission waiting room:
Key informant 2: "The cleanliness is fluctuative."
Key informant 1: "The cleanliness of this room depends on the cleaning service. The cleaning service only consists of one worker that is responsible for three rooms."
Key informant 5: "The cleaning service is already at work at 07.00 a.m. They also have midday and night shift.

Cleaning service is under the responsibility of Environment Healt Department."

16. The Easiness to Dispose Garbage in Inpatient Admission Waiting Room

The following is the deep interview on the easiness to dispose garbage in inpatient admission waiting room:
Key informant 3: "There is a garbage bin."
—Based on observation, the waiting room has three small garbage bin

17. Officers appearance in Inpatient Admission Customer Service

The following is the deep interview on officer's appearance in inpatient admission customer service:
Key informant 1: "Officers are in the front line and is obliged to have good appearance which is stated in standard operational procedure (SOP) and in the policy of the hospital."
Key informant 3: "Yes, the officers have good appearance."

18. The friendly and kind behaviour of Officers of Inpatient Admission Customer Service

The following is the result of deep interview on the friendly and kind behaviour of officers of inpatient admission customer service:
Key informant 2: "Before we serve the patient, we must address the patient kindly."
Key informant 5: "We are served kindly."

19. The Politeness of Officers of Inpatient Admission Customer Service

The following is the result of deep interview on the politeness of officers of inpatient admission customer service:
Key informant 2: "Politeness is one of the standards in customer service. The application depends on the individual."
Key informant 3 : "I have experienced being served by a polite officer and an impolite officer."
Key informant 4: "It depends on the officer. There is a polite as well as an impolite officer."

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Epidemiology of Traumatic Brain Injury in Neurosurgery Department of Tertiary Referral Hospital at North Sumatera, Indonesia

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Abstract

Introduction : Traumatic brain injury (TBI) is the most common problem that caused morbidity and mortality in the world. Epidemiology information of TBI is very important in understanding the causes and the risk factors of TBI, so that effective programs can be designed to prevent injury. This study purposed to provide overview of TBI pattern in tertiary referral hospital at North Sumatera with focus on epidemiological data of TBI pattern.

Methods : The design of this study is a retrospective, and it is done in general hospital H. Adam Malik from June-December 2018 with sample from all patient with traumatic brain injury that admited in hospital. All medical records with diagnosis traumatic brain injury will be assessed for several variables as age, gender, etiology, severity, length of stay and outcome.

Results : During the period of study, 118 patients with traumatic brain injury were admitted in neurosurgery ward. The highest TBI cases was occurs in male patients with range age between 18-35 years old, and caused by traffic accident. Most patients admitted to Emergency department with GCS 13-15 and epidural hematoma was the most common lesion found in head CT scan. Length of stay in this research mostly between 1-5 days, and the mortality rate is about 16.9%, which is dominated by severe head injury.

Conclusions : Head injury mostly found in male with productive age, and traffic accident be the most common caused. Severe head injury still have quite high mortality rate.

Introduction

Traumatic brain injury (TBI) is the most common problem that caused morbidity and mortality in the world. Morbidity caused by TBI is one of socioeconomic burden for family and country. TBI is prevalent in low, middle, and high-income country and can affects to all ages. TBI can be caused by many factors but the most common is falls, being struck by or against n object, traffic injury, and assaults.[1,2]

Incidence of TBI in worlwide was estimated 69 million lives with the highest in Western Pacific and Southeast Asia countries. The prevalence of TBI in Indonesia according to Riskesdas 2007 is 7,5% from all diseases and increase to 8,2% in 2013. Three provinces with the highest prevalence of TBI are Papua (1%), North Sumatera (0,9%), and Bangka Belitung (0,8%). According to National Center for Injury Prevention and Control, the highest rate of TBI was found in older adults (more than 75 years old) and dominated by male than female.[2,3]

Epidemiology information of TBI is very important in understanding thc causes and risk factors so that effective programs can be designed to prevent and bring down injury. Various report claimed that TBI Epidemiological pattern has been changing lately. This study purposed to provide overview of TBI pattern in tertiary referral hospital at North Sumatera with focus on epidemiological data of TBI pattern.

Materials and methods

This was a retrospective study of all patients with head injury at neurosurgery department of H. Adam Malik general hospital from June to December 2018. The hospital is tertiary referral hosptial located in Medan, North Sumatera, Indonesia with bed capacity of 720. North Sumatera has 14.42 million populations. This study was approved by the Health Research Ethical Committee Medical Faculty of Universitas Sumatera Utara / H. Adam Malik General Hospital.

All medical records of TBI patients from neurosurgery department were assessed for several variables as age, gender, etiology, severity, length of stay and outcome. The severity category was based on Glasgow coma scale (GCS) measurement in emergency department i.e mild TBI (GCS 13-15), Moderate TBI (GCS 9-12), and Severe TBI (GCS $\leq$8). Exclusion criteria for this study as death on arrival and brain injury due to cerebrovascular disease, seizure, or psychiatric problems. All data will be presented descriptively as frequency and percentage in tables.

Results

During the period of study, 118 patients with traumatic brain injury were admitted in neurosurgery ward. From all patients with TBI, 89 (75.4%) were males and 29 (24.6%) were female so the ratio is 3.1:1. Patients' age were ranged every 10 years with highest frequency of 43 (36.4%) was found in the age range of 18-35 years and followed by 27 (22.9%) in the age of >56 years. Based on etiology of TBI, the most common cause was road traffic accident (n= 95, 80.5%) then followed by falls (n= 15, 12.7%) and violence (n= 8, 6.8%).

Table 1. Characteristics of patients

The patients whose GCS category were stated mild TBI, which constituted 78 (66.1%) were the highest frequency, followed by moderate TBI constituted 29 (24.6%). Based on brain lesion, the highest frequency was epidural hematoma for 40 (3.9%) then followed by intraparenchymal hemorrhage for 33 (28%). The highest outcome of patients of study was discharged (n= 84, 71.2%) then followed by mortality (n= 20, 17%). Length of stay in this study were ranged every 5 days with highest frequency of 45 (38.1%) was found in the length stay of 1-5 days and followed by 37 (31.4%) in the length stay of 6-10 days.

Discussion

Total of traumatic brain injury cases from neurosurgery department of H. Adam Malik general hospital in 2010 showed 1627 cases which 1021 cases are mild TBI, 444 cases are moderate TBI, and 162 cases are severe TBI. Compare to our data, there were significant reduction TBI cases from 1627 cases in 12 months to 118 cases in 6 months. North Sumatera only has 9 neurosurgeons in 2010 but in 2019 this amount have increased two times into 21 neurosurgeons. Enhancement of neurosurgery service in secondary healthcare at North sumatera decreaseing referral need to tertiary referral hospital.[4]

Several studies showed that TBI in both developing and developed countries dominate by male than female. This study also showed that males were more affected than females. While most of TBI found in productive age between 21-40 years. In this study, the highest frequency of TBI was also found in productive age, between 18-35 years. This might be caused by the fact that males with productive age are more active in daily activities that prone to head injury such as vehicle operation and working on heights.[5,6]

Road traffic accident has the highest frequency for the cause of TBI in this study. Traffic accident was also the most common causedof TBI in developing country. Meanwhile, fall and assault were the most prevalent cause of TBI in developed country. This can be caused by better road network and good implementation of traffic rules.[6,7] Mild Head injury has the highest frequency of TBI from this study and other studies also reported the same result.[7, 8]

The mortality rate for TBI was declined significantly over decade from 39% in 1984 to 27% in 1996. Mortality rate in this study was 16,9% which mean better treatment over years but still two times higher than

US National Health Statistics Reports.[9,10] Length of stay in this study commonly under 10 days is 69,5% and under 15 days is 90.7%. Study from US and Canada reported different length of stay which average length of stay in US is 7.3 days and in Canada is 11.7%. Several important factors that can prolonged length of stay are age, gender, GCS, injury severity, and ventilator usage.[10,11]

Being a retrospective study could have loss of important information that might be relevant. This is limitations of present study. Retrospective study has disadvantage of poor recording due to relied on accuracy of written records. This can happen because our record still paper based so poor keeping is common.

Conclusion

TBI patients were dominate by male with range from 18-35 years. Traffic injury was the most common cause of TBI. Most of TBI patients were mild with length of stay less than 10 years. Mortality rate in our study is 16.8%.

Conflicts of interest

There are ni conflicts of interest

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Table 1. Characteristics of patients

Variable	Total	Percentage
Usia (tahun)		
0-17	22	18.6
18-35	43	36.4
36-55	26	22.1
>55	27	22.9
Gender		
Male	89	75.4
Female	29	24.6
Etiology		
Traffic injury	95	80.5
Fall	15	12.7
Violence	8	6.8
GCS		
Mild	78	66.1
Moderate	29	24.6
Severe	11	9.3
Lesion type		
Epidural Hematoma	40	33.9
Subdural Hematoma	15	12.7
Intraparenchymal Hemorrhage	33	28.0
Subarachnoid hemorrhage	7	5.9
Skull fracture	13	11
Mix lession	10	8.5
Length of stay (days)		
1-5	45	38.1
6-10	37	31.4
11-15	25	21.2
16-20	4	3.4
21-25	1	0.8
26-31	6	5.1
Outcome		
Discharged	98	83.1
Died	20	16.9

Case Report : Generalized Myasthenia Gravis

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Keywords : Myasthenia Gravis, Generalized
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Abstract

Generalized myasthenia gravis is a rare case of autoimmune wherein the antibodies destroy the post-sinaptic acetylcholine receptors at skeletal muscle's neuromuscular junctions. The clinical presentation is specific distributin of motoric deficit without sensoric deficit which diminished with rest and worsens with excessive use. We report a case of a woman 52 yo with symptoms of ptosis, diplopia and dificulty of swallowing. Repetitive nerve stimulation showed >10% decrement and prostigmin test was positive. The patient was treated and showed clinical improvement.

Introduction

Myasthenia gravis is a rare case of autoimmune in which the antibodies destroy the post-sinaptic acetylcholine receptors at skeletal muscle's neuromuscular junctions. It has a prevalence of 1.7-21.3 out of 1.000.000 people. The incidence is higher on women than men in ≤ 50 years old community (7:3), yet at >50 years old, men have more risk (3:2)[1]. Clinically, myasthenia gravis is divided into 2 subgroup : ocular and generalized. Patients with ocular myasthenia gravis only present with diplopia and ptosis. On the other hand, generalized myasthenia manifested as extraocular symptoms such as dysphonia, dysphagia, and even dyspnea[1,2].

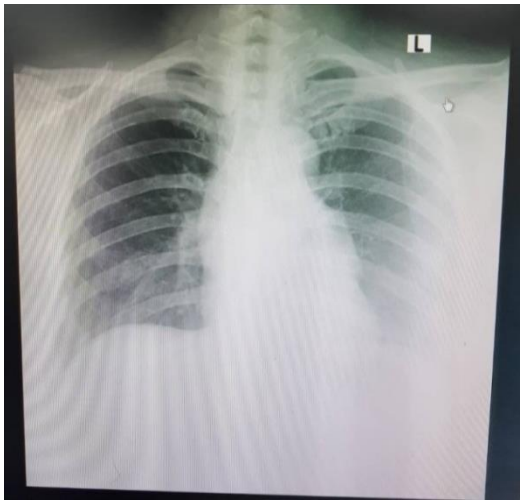
Case

In this case, 52 year old woman came to our outpatient department with difficulty of opening her right eye since 10 days ago which worsens gradually within 3 days. She also had diificulty gazing right and up, causing her to turn her neck. She could not see clearly due to double vision. She also had nasally and slurred speech, difficulty swallowing liquid and using straws hence often getting choked, diificulty chewing and closing her jaws since 2 months ago. All of her symptoms were getting worse at mid-day after activity, yet diminished with rest. She usually felt fine when she woke up in the morning. There was no limb or generalized weakness, dysarthria, pain, tingling, nor difficulty of breath.

Patient and family members never had similar symptoms. She had a history of uncontrolled hypertension and diabetes mellitus. She did not smoke but became a passive smoker. She rarely consumed tinned food.

Physical examination showed high blood pressure 140/90 mmHg. Cranial nerve examination showed she had heavy right eye ptosis 4mm/1mm. She also had 3rd, 6th, 7th, and 9th cranial nerve paresis. Specific wartenberg, simpson and counting tests were done and the results were positive. The patient had no sensoric dysfunction. Limb motoric and deep tendon reflexes were normal. Meningeal signs and pathological reflexes were not found.

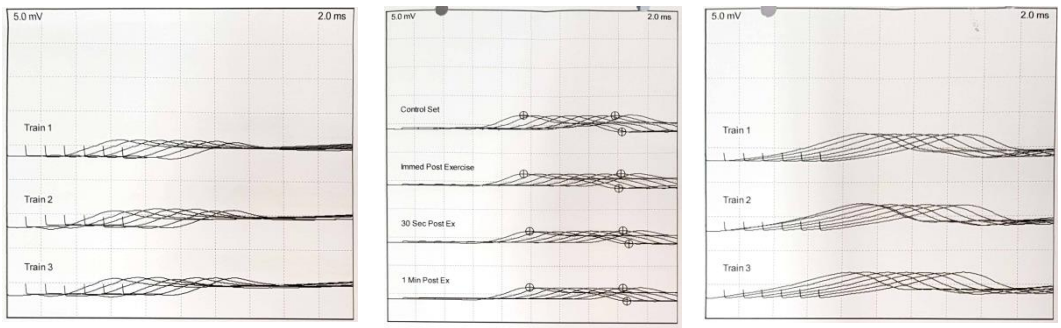
The patient was diagnosed with generalized myasthenia gravis and further diagnostic tests were done. Chest xray was done, no abnormality was found other than aorta elongation. Blood test was done and showed normal result. The patient was admitted into the ward. She was given ramipril and metformin. In order to prevent masking effect, myasthenia gravis medication was not given yet.



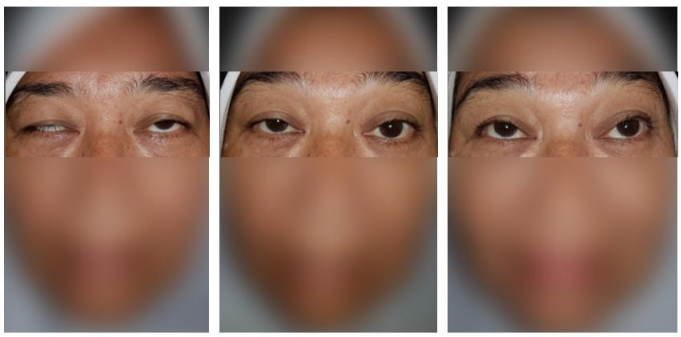
Picture 1. Chest postero-anterior Xray with aorta elongation.

On the next day, the patient could see without double vision and speak normally. She could also drink from a water bottle without choking. However, she still had difficulty opening her right eye. She had her period the day before. Physical exam showed improvement of her ptosis 3mm/1mm. Her HbA1C test showed uncontrolled diabetes mellitus. Repetitive nerve stimulation test result was decrement >10% and prostigmin test was positive confirming myasthenia gravis diagnosis. She was given pyridostigmine 60 mg three times a day.

On the following day, the patient had significant improvement of her ptosis 2mm/1mm. Her previous symptoms have diminished. She was admitted out of the ward with a control appoinment at next week.



Picture 2. Repetitive Nerve Stimulation Test (from left to right): A) Right orb oculi, B) Median Repetitive Stimulation, C) Right trapezius repetitive stimulation test



Picture 3. Right eye ptosis (from left to right): A) Before treatment, B) The first day after treatment, C) The second day after treatment.

Discussion

Muscle motoric weakness without sensory and deep tendon reflexes deficit which worsens with repetitive use and diminished with rest is a specific symptom of myasthenia gravis. In this patient, the acetycholine receptor (AChR) in post-synaptic membrane at neuromuscular junction was decreased. This phenomenon was due to the autoimmune response mediated by the anti- AChR by 3 mechanisms : AChR turnover acceleration, AChR active location blockade and damage at post-synaptic muscle membrane[2]. The neuromuscular junction of myasthenic patient had swallow post-synaptic folds and wide synaptic cleft. These mechanisms reduced the eficiency of her neuromuscular transmission, hence causing muscular weakness. The number of released acethylcholine (ACh) will be reduced during repetitive activity (presynaptic rundown), thus causing the patient felt healthy in the morning and became weak after repetitive activity (myasthenic fatigue).

The patient was diagnosed as generalized myasthenic gravis because aside from ocular symptoms, she also had bulbar symptoms. According to her story, she had the first symptoms since 2 months ago. Her disease exacerbated 10 days ago due to stress and excessive physical activity. Wartenberg, simpson and counting tests were special physical exam to narrow down the diagnosis. Ice pack eye test is a useful bedside test that can aid in the differentiation of MG and should have been done[3]. It is a cheap, safe, and quick test. The test consists of the application of covered ice to the eyes for 2-5 minutes. If positive, the patient no longer has diplopia or a raise of 2 mm of the palpebral fissure. The mechanism behind this test is that by cooling the tissues, more specifically the skeletal muscle fibres, the activity of the acetylcholinesterases are inhibited. Myasthenic Gravis Composite (MGC) scale should have also been done in order to assess the clinical severity of this patient. Increase of ≥ 3 points of MGC scale showed significant clinical improvement[4].

Laboratory examination played an important role in diagnosing myasthenia gravis. The current gold standard are anti-AChR and anti-MuSK antibody tests. Antibody testing was not done due to limitation of source.

Decremental > 10-15% in repetitive nerve stimulation test can be found in myasthenia gravis patient. Prostigmin test was done by intramuscular injection of 3cc prostigmin methysulphate and diminished clinical symptoms showed positive result.

There were diabetes mellitus and hypertension as comorbids. The relationship between myasthenia gravis and diabetes mellitus was still unclear. However, myasthenia gravis treatment might induced diabetes mellitus[5]. Yet, in this case, the patient had diabetes mellitus before she received corticosteroid treatment. On the other hand, myasthenia gravis might cause diffuse cholinergic dysfunction, hence causing autonomic dysfunction. This mechanism might have increased the patient's risk for hypertension[6].

The differential diagnoses of this patient were Lambert-Eaton Myasthenic Syndrome (LEMS), botulism and intracranial mass lession. However, repetitive nerve stimulation test showed incremental results in LEMS, botulism patients present with autonomic symptoms, and intracranial nerve lesion might present with vomiting and other neurological deficits.

According to myasthenia gravis algorithm, patients should receive pyridostigmine as first line drug. Pyridostigmine inhibits acetylcholinesterase in the synaptic cleft thus slowing down the hydrolysis of acetylcholine. If symptoms persisted, clinicians should evaluate for thymectomy[7]. Neck CT scan should have been done to detect thymoma. If the patient refused or symptoms still persisted, immunosuppresive drugs should have been given[8,9].

The patient's prognosis was good. However, most myasthenia gravis patients did not have full remission[2]. Patients should be educated to avoid exacerbating factors. Patient should also be told regarding myasthenic crisis symptoms and management.

Conclusion

Generalized myasthenia gravis is a rare disease. The primary management are anti-acethylcholinesterase drugs. Early diagnosis and treatment might increase patient's chance for full remission.

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Case Report : Caecal Endometrios is Causing Acute Small Bowel Obstruction

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Abstract

Introduction: Endometriosis in bowel is rare condition, about 12% of endometriosis cases. Most of bowel endometriosis rising in the rectosigmoid (90% of bowel endometriosis). Incidence of caecal endometriosis is very low (<5% of bowel endometriosis) and almost never causing acute small bowel obstruction(0.1-0.7%). The aim of this paper is to show that although bowel obstruction caused by caecal endometrios
is is difficult to diagnose as it is rare, and may require laparotomy to make definite diagnosis, but it should be considered in infertile female patient.

Case: 37 years old woman infertile woman with intestinal obstruction with pre-operative diagnosis total acute small bowel obstruction caused by right colonic mass, with sepsis as the complication. Before the acute small bowel obstruction she complained of chronic right lower quadrant pain with chronic constipation alternate with chronic diarrhea, symptoms that happened both in bowel endometriosis and colorectal malignancy. She also complained of chronic pelvic pain and dysmenorrhea. She has been married for 10 years with no child. The patient was never diagnosed with endometriosis and never seek medical attention for the infertility and the chronic pelvic pain. The patient underwent Abdominal CT Scan, with result: massive small bowel obstruction, and caecal mass that causing acute small bowel obstruction. Diagnosis of Acute small bowel obstruction due to right colonic mass was made and emergency exploratory laparotomy was performed the patient.

Methods: During the laparotomy, mass at caecum and ileocaecal that causing massive small bowel obstruction was found and standard right hemicolectomy and temporary mucousfistula ileostomy was performed.

Result: The patient recovered well, discharged on 7th day post op. The pathology examination showed ectopic endometriosis lesions in caecum and ileocaecal valve. The histopathology also confirmed with the immunohistochemistry, in which positive ER, PR, CD 10 and CD7 was found the ileocaecal and caecal mass. In the second operation, reanastomosis of the ileum was done 3 months after the first operation. The chronic pelvic pain is decreasing dramatically after the first and second operation.

Conclusion: Although bowel obstruction caused by caecal endometriosis is an extremely rare cause of intestinal obstruction but it should be considered as a cause in infertile female patient to reduce morbidity and mortality, to reduce stoma creation and to promote resection completeness.

Case Illustration

37 years old patient came to ER with chief complaint of difficulty to defecate and pass gas within the last 3 days, acoompanied with distended and colic intermittent abdominal pain. Patient complained of chronic intermittent diarrhea with blood and chronic pelvic pain. The patient has history of infertility (10 years of marriage without child) with dysmenorrhea.The patient has never seek any medical attention for the gynecological problem. At arrival : BP 120/90mmHg, HR 110x/minute, RR 24x/minute, Temp 37 Celcius degree. Laboratory finding : Hb 12.5gr/dL, WBC : 24.000/mm3, Ht 36%, Platelet 305.000/mm3.Other lab finding is within normal limit.

Radiologic Finding

Abdominal x-ray confirmed that patient has obstructive ileus with step ladder pattern sign with high level obstruction/small bowel obstruction(Gambar 1-3). Abdominal CT Scan with IV contrast was done to seek the cause of obstruction, with conclusion the cause is mass in the right colon(figure 4 and 5). No other cause of obstruction and other abnormalities found in the abdominal CT Scan.

Surgical Evaluation and Specific Finding

Patient underwent emergency exploratory laparotomy in which we found massive dilatation of small bowel caused by palpated intraluminal mass in caecal region, with collapsed large bowel(figure 6).
Standard right hemicolectomy(removeal of terminal ileum until proximal transverse colon) was done and ileostomy mucousfistula was constructed in this patient. Patient recovered well within 1 week in the hospital and then she was discharged without complication.

Histopathologic Finding

After operation, specimen was opened and irregular mass in caecum and ileocaecal valve (Figure 7) with appropriate microscopic finding, with positive endometrial tissue in bowel (Figure 8).
This histopathologic finding was proven with immunohistochemistry staining of Estrogen Receptor(ER) and Progesteron Receptor(PR) also cytokeratin (CK) 7 and CK 10. Endometrial glands are stained by ER, PR and CK7 staining, bowel epithelial was stained with CK 10(figure 9).

Post Operative Follow Up

Patient has recovered well, and discharged 1 week after the operation. In the 3rd month, the patient was done ileal reanastomosis and chronic pelvic pain is reduced dramatically in this patient.

Discussion

Endometriosis is gynecological condition in which the functional endometrium is found outside the uterus.[1] Endometriosis is found in 6-10% women in reproductive age, and only 50% of the endometriosis patient shows pelvic pain, abnormal period, and infertility caused by the endometriosis.[2] Frequent affected location are pelvic peritoneum, ovarium and rectovaginal septum.[2] Infrequent location of the endometriosis are pleura, pericardium, small bowel and large bowel, and other tissues.[2]

Bowel endometriosis are the most frequent site of endometrial location outside pelvis, about 12% of the extrapelvic case. [3,4] And the lesion in the bowel causing bowel obstruction is very rare only 0.1 until 0.7%, and most of them are found in rectosigmoid and rarely found in caecum.[5]

Etiology of endometriosis are not truly understood. Usually the retrograde menstruation is commonly mentioned but not all women with retrograde menstruation has endometriosis. [2] Another theory mentioned vascular dissemination, colonic metaplasia and autoimmune disease [5]
Endometriosis act like endometrial tissue in uterine and responded to ovarial hormone although attached to other organ. Even endometriosis could implanted and formed cyst or nodule(endometrioma).[2] In the attached location, endometriosis could cause bleeding, fibrosis and pain(as in this patient). [5]

As mentioned above, bowel endometriosis rarely causing obstruction(0.1-0.7% of all cases). This is because bowel endometriosis usually in the submucous layer of the bowel only, and not infiltrating deeply to the bowel wall. [5] In general the patient complains of non-specific symptoms like pain, nausea, vomiting, bloated abdomen, diarrhea and constipation and all these symptoms usually cyclical(proliferation of endometrial tissue is depend on ovarial hormones). [2,6]

Very rarely endometriosis proliferate, causing fibrosis and strictures of the bowel and causing bowel obstruction. [3,4,5]

Diagnosis of bowel endometriosis is not easy to make, because a lot of GIT symptoms are alike, and in the small lesions it is not specific. In the large lesion, the symptoms is like other bowel tumor, and the abdominal CT Scan usually large lesion will formed thickening of the bowel wall(like any other bowel tumor). [9] Transvaginal USG and Pelvic MRI could give clear picture to see any endometrioma but it is hard to see the real bowel adhesion caused by the endometriosis itself. [2] Endoscopic evaluation usually don't show any pathologic lesion unless the lesion is arising in the bowel mucosa and could be biopsied by endoscopy. [8] The gold standard of diagnosis is laparoscopy(direct visualization) and biopsy via laparoscopy, which could give direct view of pelvis and bowel resection could be done if needed. [8]

In this patient, endometriosis is not considered as cause of obstruction preoperatively because all of the sign and symptoms could be find in the obstructed bowel due to right colonic tumor. Endoscopy is not done in this patient because she already in obstructed bowel condition, and abdominal CT Scan already give clear explanation of obstruction and the cause of it (right colonic mass). Also laparoscopy could not be done because she is in total bowel obstruction, with very distended abdomen. The surgeon decided for emergency exploratory laparotomy in which caecal mass is found. In the histopathology and immunohistochemistry staining was found that the mass is an endometrioma.

Empiric therapy could be given for dysmenorrhea and chronic pelvic pain in patient suspected endometriosis. The first line therapy usually NSAID combined with cyclical oral continuous oral contraception. [9,10] Another option is including gonadotropin releasing hormone (GnRH) agonist and aromatase inhibitors.[2,6] These medications works by suppressed the inflammation, suppressed and disturbing the ovarial hormones production causing hypoestrogenic, endometrial atrophy and causing olygomenorrhea and amenorrhea.[2,11] Surgery option including resection and adhesiolysis is offered in the deep infiltrating endometriosis (DIE). In the patient with DIE and/or the medicine could not work for endometriosis, surgery is an option to be considered. [2,6,12] The success of operation depends on the completeness of resection, so the success is very depended on the pre-operative diagnosis. Pre-operative diagnosis made before obstruction could also reduce morbidity and mortality of the patient, and also reduce stoma creation like in this patient. [13]

Conclusion

Although bowel obstruction caused by caecal endometriosis is an extremely rare cause of intestinal obstruction but it should be considered as a cause in infertile female patient to reduce morbidity and mortality, to reduce stoma creation and to promote resection completeness.

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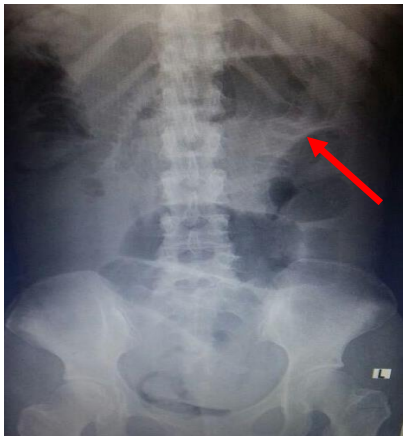

Figure 1. Supine abdominal x-ray shows small bowel dilatation with herring-bone sign

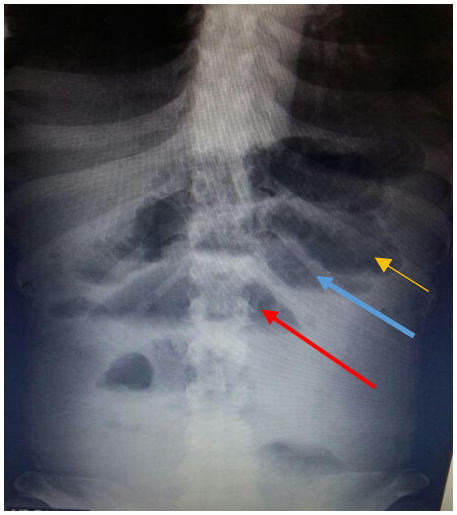

Figure 2. Erect abdominal x-ray shows classic step ladder pattern, a pathognomonic sign for acute bowel obstruction

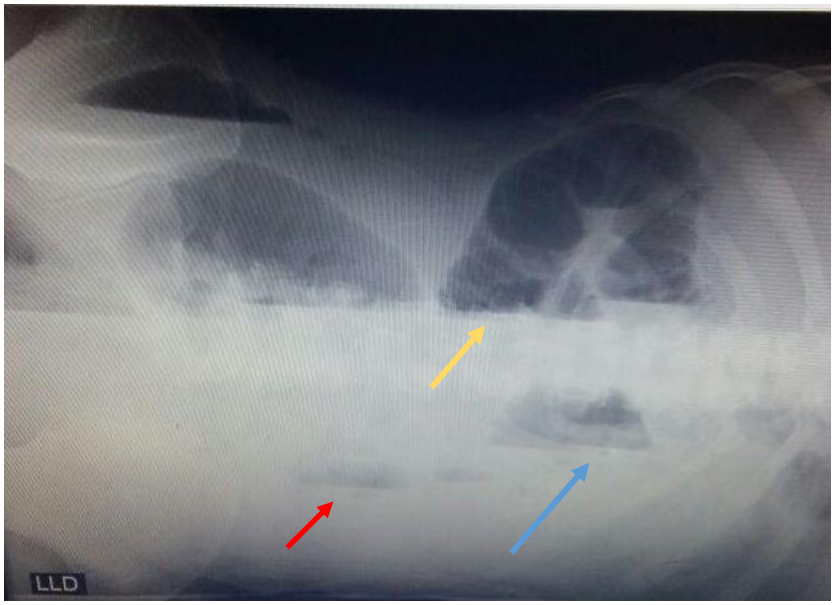

Figure 3. X-ray of Left Lateral Decubitus shows multiple air fluid level and step ladder pattern

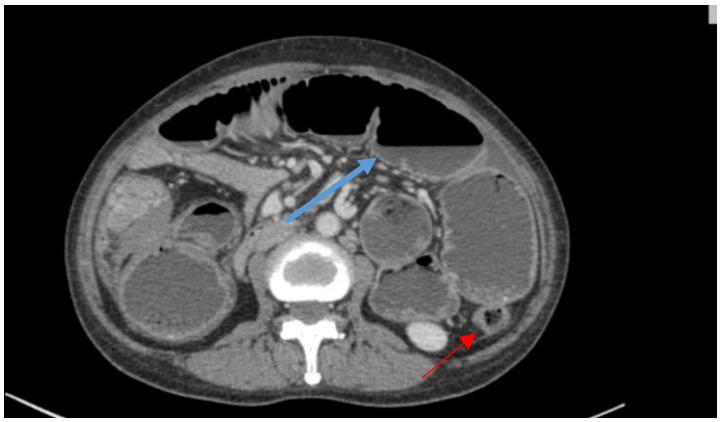

Figure 4. Abdominal CT Scan in saggital plane shows massive dilatation of small bowel (blue arrow) with collapsed large bowel (red arrow)

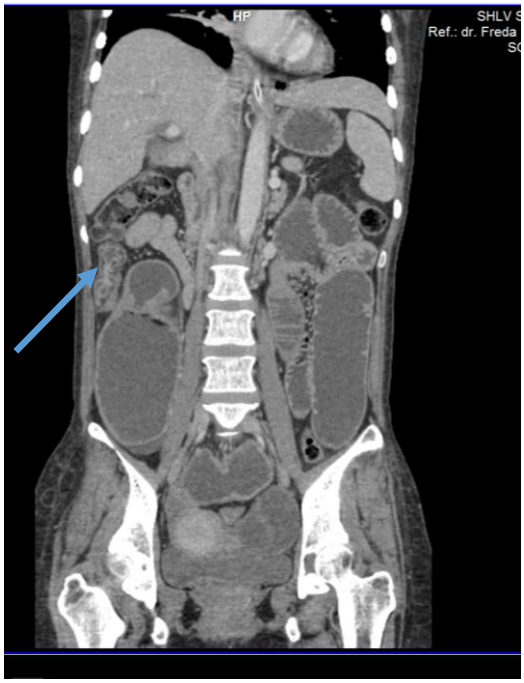

Figure 5. Abdominal CT with IV contrast in coronal section, shows massive dilatation of small bowel with collapsed right large bowel (blue arrow)

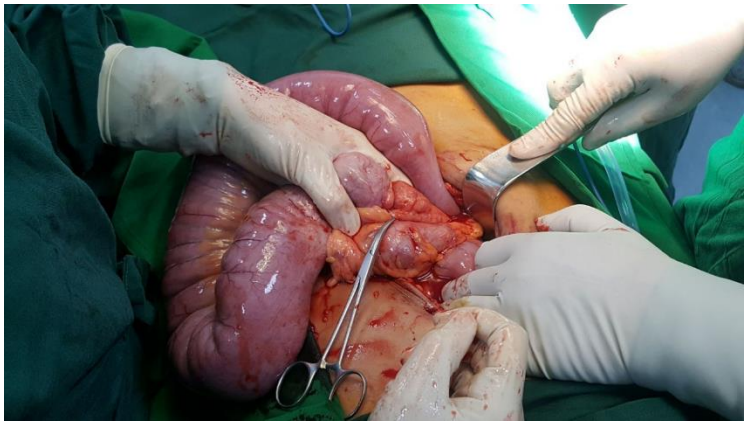

Figure 6. Intraoperative findings indicate massive small bowel obstruction with a mass in the Caecum (appointed with clamps)

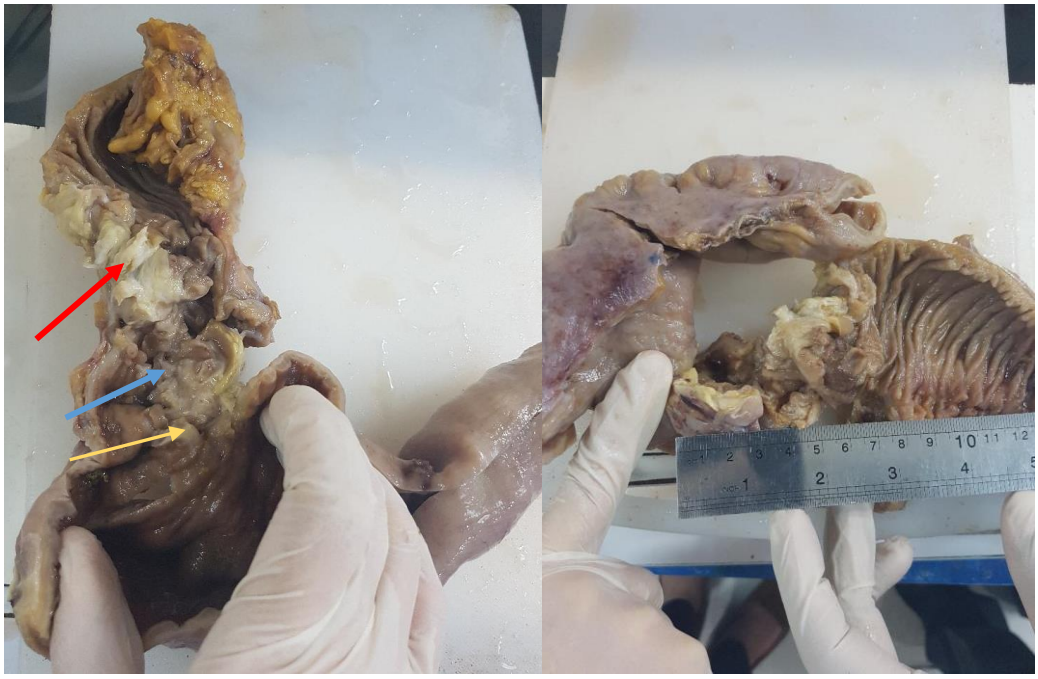

Figure 7. Macroscopic finding of the tissue shows infiltrative endometriosis in caecum(red arrow) and ileocaecal valve (blue and yellow arrow)

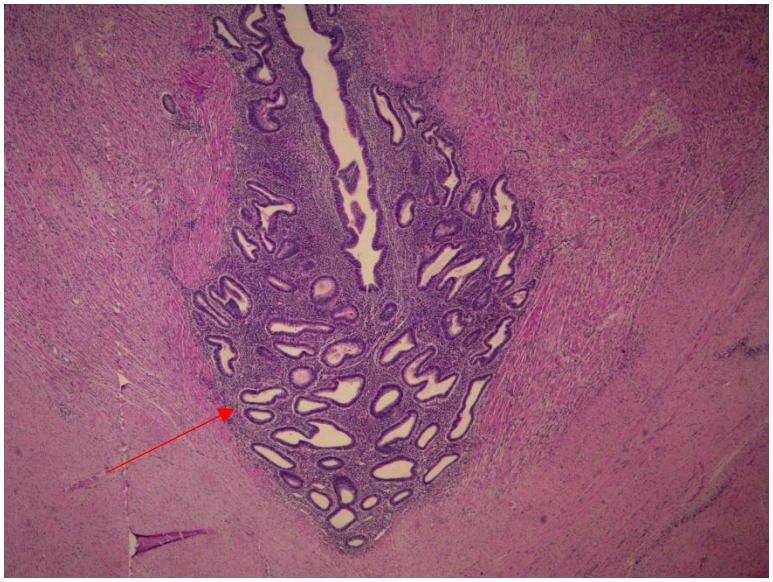

Figure 8. Histopathologic finding shows invasive endometriosis to normal caecal tissue

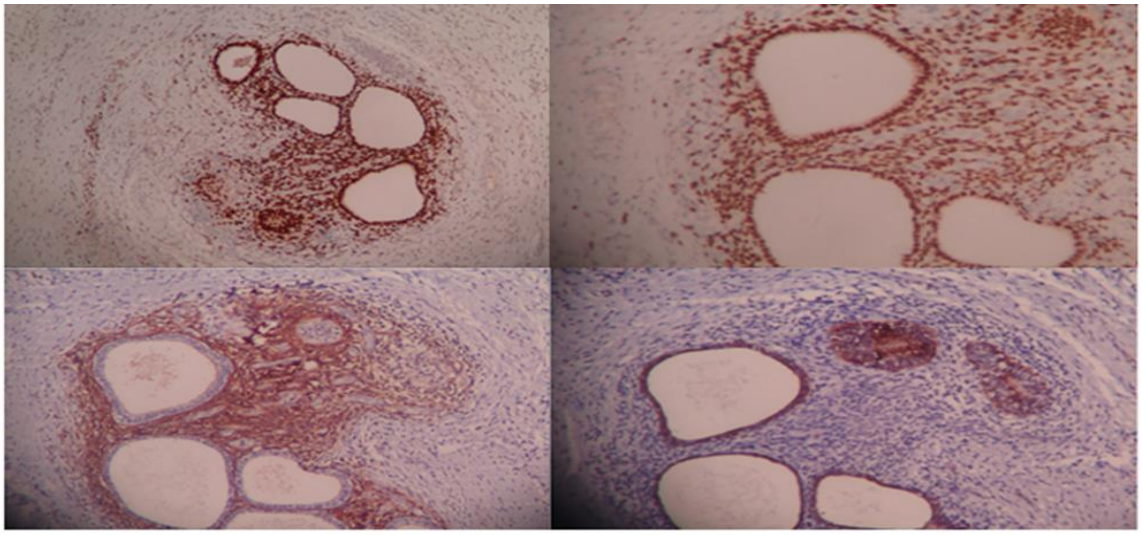

Figure 9. Immunohistochemistry staining shows positive result for ER, PR, CK 7 confirmed of endometrial tissue and CK 10 that confirmed bowel epitelial