



**7<sup>th</sup> Biannual International Symposium  
on Nasopharyngeal Carcinoma 2015**

**Royal Ambarrukmo Hotel  
Yogyakarta, 4 - 6 June 2015**

***Words from the chair***

Dear colleagues,

It is a great pleasure to welcome you to the 7<sup>th</sup> International Biannual Symposium on Nasopharyngeal Carcinoma, in Yogyakarta-Indonesia on 4-6 June 2015. Series of the meetings have gathered experts and scientists on NPC from the west and east part of the world for more than 10 years.

This year symposium aims to communicate recent findings on NPC research in the field of basic science, clinical and translational science, and epidemiology. During the symposium we are hosting series of speakers in the form of oral and poster presentations, as well as clinical discussions. Importantly we also wish to discuss problems and possible solutions for NPC clinical management in developing countries.

Hope we will have fruitful discussions

Thank you for attending this event

Thank you for your valuable scientific contributions

***Johan Kurnianda, MD***

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## Scientific Schedule

Day I. 4 June 2015

### Etiology of NPC

TIME	TOPICS	ABSTRACT NUMBER
08.00 - 08.30	Registration	
08.30 - 09.00	Opening	
09.00 - 09.30	<b>Keynote address</b> Professor I. Bing Tan, MD, PhD (Netherlands Cancer Institute/AVL Hospital Amsterdam, NL-Universitas Gadjah Mada Yogyakarta Indonesia)	PL-01
09.30 - 10.00	Cofee break	
10.00 - 11.20	<b>PLENARY 1 : Epidemiology (World distribution, Molecular epidemiology, and Risk factors)</b> Chair Person: Allan Hildesheim, Ph.D (Chief Infections and Immunoepidemiology Branch, NCI, US)	
10.00 - 10.20	<b>NPC international incidence and risk factors</b> Ellen Chang, Sc.D (Senior Managing Scientist, Stanford Cancer Institute, LA, CA,USA)	PL-02
10.20 - 10.40	<b>Familial nasopharyngeal carcinoma and the use of biomarkers</b> Professor Chien-Jen Chen (Genomics Research Center, Academia Sinica; and Graduate Institute of Epidemiology and Preventive Medicine, National Taiwan University, Taipei)	PL-03
10.40 - 10.50	<b>Hospital-based frequency and clinical characteristics of patients with nasopharyngeal carcinoma patients in Indonesia</b> Marlinda Adham, MD, PhD (Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia)	OP-01
10.50 - 11.00	<b>Epstein-Barr Virus Seromarkers and Risk of Nasopharyngeal Carcinoma: the Gene-Environment Interaction Study on Nasopharyngeal Carcinoma in Taiwan</b> Yin Cu Chien (Genomics Research Center, Academia Sinica, Taipei)	OP-02
11.00 - 11.10	<b>Familial Tendency and Environmental Co-factors of Nasopharyngeal Carcinoma: the Gene-Environment Interaction Study on Nasopharyngeal Carcinoma in Taiwan</b> Wan-Lun Hsu (Genomics Research Center, Academia Sinica, Taipei)	OP-03
11.10 - 11.20	<b>Nasopharyngeal carcinoma (NPC) case control study in Indonesia</b> Jajah Fachiroh, PhD (Universitas Gadjah Mada, Yogyakarta, Indonesia)	OP-04
11.20 - 12.05	<b>Industrial Lunch Symposium: Supportive Care in Head and Neck Cancer: Focus on Pain and Anemia Management</b> Dr. dr. Aru W. Sudoyo. Sp.PD-KHOM, FINASIM (Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta)	
12.05 - 12.50	Lunch	

12.50 - 14.40	<b>PLENARY 2: Genetics and Epigenetic</b> Chair Person: Ellen Chang, Sc.D (Senior Managing Scientist, Stanford Cancer Institute, LA, CA, USA)	
12.50 - 13.10	<b>Genetic susceptibility risk factors for sporadic and familial NPC: recent findings</b> Allan Hildesheim, PhD (Chief Infections and Immunoepidemiology Branch, NCI, US)	PL-04
13.10 - 13.30	<b>Genetic and Genomic Studies of Nasopharyngeal Carcinoma</b> Professor Jinxin Bei (State Key Laboratory of Oncology in South China, Sun Yat-sen University Cancer Center, Guangzhou, China)	PL-05
13.30 - 13.50	<b>Genetic and Environmental Risk Factors for Nasopharyngeal Cancer in South East Asia</b> James McKay, PhD (IARC, Lyon, France)	PL-06
13.50 - 14.10	<b>Characterization of the NPC methylome identifies aberrant epigenetic disruption of key signaling pathways and EBV-induced gene methylation</b> Professor Qian Tao (School of Biomedical Sciences, The Chinese University of Hong Kong, China)	PL-07
14.10 - 14.20	<b>Epigenetic identification of a novel regulator of p53-signaling as a broad tumor suppressor frequently methylated in multiple tumors</b> Lili Li, Ph.D (Chinese University of Hong Kong, Hongkong)	OP-05
14.20 - 14.30	<b>Identification of Potential Tumour Susceptibility Genes in Constitutional DNA of Nasopharyngeal Carcinoma Patients with First Degree Relatives of NPC via Whole-Exome Sequencing</b> Hamidah Akmal Hisham (Institute for Medical Research, Kuala Lumpur, Malaysia)	OP-06
14.30 - 14.40	<b>The genetic susceptibility and prognostic role of TERT-CLPTM1 and genes in DNA damage pathways in NPC</b> Josephine Mun Yee Ko (University of Hongkong, Hongkong)	OP-07
14.40 - 14.55	Coffee break	
14.55 - 16.35	<b>PLENARY 3: EBV-Host Relationship</b> Chair Person: Prof. Jaap Middeldorp, PhD (VU University Hospital, Amsterdam, The Netherlands)	
14.55 - 15.15	<b>Tumor exosomes and translational research in NPC</b> Dr Pierre Busson, MD, PhD (Institut de Cancérologie Gustave Roussy, Villejuif, Cedex, France)	PL-08
15.15 - 15.35	<b>Host manipulations of the Epstein-Barr virus EBNA1 protein</b> Lori Frappier, PhD (Dept of Molecular Genetics, University of Toronto, Canada)	PL-09
15.35 - 15.55	<b>Somatic Genetic Changes in EBV-associated Nasopharyngeal Carcinoma</b> Prof. Kwok-Wai Lo (University of Hong Kong, Hong Kong)	PL-10
15.55 - 16.05	<b>Mechanism study of Ovol2 regulate the differentiation of NPC</b> Hui Qiong Han (Sun Yat-sen University Cancer Center, Guangzhou, China)	OP-8
	<b>The oncogenic role of RE1-silencing transcription factor (REST) in LMP1-expressing cancer cell lines</b> Mitsuharu Aga (Kanazawa University, Japan)	OP-9
16.05 - 16.15		
16.15 - 16.25	<b>Epstein-Barr virus miR-BART20-5p regulates cell proliferation and apoptosis by targeting BAD</b> Suk Kyeong Lee (The Catholic University of Korea, Seoul, Republic of Korea)	OP-10
16.25 - 16.35	<b>Comparison of circulating biomarkers in patients with nasopharyngeal carcinoma</b> Min Han Tan (Institute of Bioengineering and Nanotechnology, Republic of Singapore)	OP-11
16.35 - 18.00	Poster reception (high tea reception)	
18.00 - 19.30	<b>NPC Consortium Meeting</b> Coord: Allan Hildesheim, PhD	

Day II. 5 June 2015

Screening, Diagnosis, and Treatment of NPC

TIME	TOPICS	ABSTRACT NUMBER
08.00 - 09.30	<b>PLENARY 4: NPC Screening and Awareness</b> Chair Person: Prof. Mu-Sheng Zheng, MD, PhD (Cancer Institute, Sun Yat-sen University, China)	
08.00 - 08.20	<b>Preliminary screening results for nasopharyngeal carcinoma with ELISA-based EBV antibodies in southern China</b> Su-Mei Cao, MD, PhD (Sun Yat-sen University Cancer Center, China)	PL-11
08.20 - 08.40	<b>EBV array platform to screen for EBV antibodies associated with NPC and other EBV-associated disorders</b> Prof. Denise Doolan (QIMR Berghofer Medical Research Institute, The University of Queensland, Australia)	PL-12
08.40 - 09.00	<b>The nasopharyngeal carcinoma awareness program in Indonesia</b> Sagung Rai Indrasari, MD, MSc (Universitas Gadjah Mada/Dr. Sardjito Hospital Yogyakarta, Indonesia)	PL-13
09.00 - 09.10	<b>Long Term Effects of NPC Screening</b> Mingfang Ji (Cancer Research Institute of Zhongshan, Guangdong, China)	OP-12
09.10 - 09.20	<b>The Usage Of Traditional, Complementary, And Alternative Medicine Of Newly Diagnosed Patients With Nasopharyngeal Carcinoma In Yogyakarta, Indonesia</b> Jose Schutter (The Netherlands Cancer Institute, Amsterdam, The Netherlands)	OP-13
09.20 - 09.30	<b>Risk prediction of Nasopharyngeal Carcinoma by detecting host genetic and Epstein-Barr Virus variation in saliva</b> Qian Cui (Sun Yat-sen University Cancer Center, Guangzhou, China)	OP-14
09.30 - 10.00	Coffee break	
10.00 - 11.30	<b>PLENARY 5: Clinical Diagnosis of NPC</b> Chair Person: Prof. Soehartati Gondhowidjojo, MD (Universitas Indonesia/Dr. Cipto Mangunkusumo Hospital)	
10.00 - 10.20	<b>Advances in MR imaging in NPC</b> Prof. Ann D. King, MB BCH, MRCP, FRCR, FHKCR, FHKAM (The Chinese University of Hong Kong, China)	PL-14
10.20 - 10.30	<b>Patterns of care study in Turkish nasopharyngeal cancer patients (NAZOTURK): A Turkish Radiation Oncology Association Head and Neck Cancer Working Group Study</b> Prof. Enis Oyar (Departments of Radiation Oncology of Acibadem University, Ankara, Turkey)	OP-15
10.30 - 10.40	<b>New suggestions of UICC/AJCC staging system for nasopharyngeal carcinoma in era of IMRT: recombination of T and N stages</b> Yun Fei Xia (Sun Yat Sen University, Guangzhou, China)	OP-16

10.40 - 11.30	<b>Panel discussion: Challenges of NPC diagnosis in developing countries</b> Chair Person: Alan Khoo Soo Beng, MD (Institute for Medical Research, Kuala Lumpur, Malaysia) a. Yussy Afriani Dewi, MD (Universitas Padjajaran/Dr. Hasan Sadikin Hospital, Bandung, Indonesia) b. Sagung Rai Indrasari, MD, MSc (Universitas Gadjah Mada/Dr. Sardjito Hospital Yogyakarta, Indonesia)	
11.30 - 13.15	Lunch and Friday praying	
13.15 - 14.25	<b>PLENARY 6: Primary Treatment of NPC and Prognostic Markers</b> Chair Person: Alan Khoo Soo Beng, MD (Institute for Medical Research, Kuala Lumpur, Malaysia)	
13.15 - 13.35	<b>Current advances and future direction in NPC management</b> Prof. Brian O'Sullivan, MB Bch BAO, FRCPC (University of Toronto, Toronto, Canada)	PL-15
13.35 - 13.55	<b>Management for Juvenile NPC</b> Prof. Enis Oyzar (Departments of Radiation Oncology of Acibadem University, Ankara, Turkey)	PL-16
13.55 - 14.05	<b>Long term outcome of intensity modulated radiotherapy in nasopharyngeal carcinoma in National Cancer Centre Singapore</b> Kiattisa Sommatt (National Cancer Centre Singapore, Singapore)	OP-17
14.05 - 14.15	<b>Establishment and Validation of Prognostic Nomograms for Endemic Nasopharyngeal Carcinoma</b> Prof. Hai Qiang Mai (Sun Yat Sen University, Guangzhou, China)	OP-18
14.15 - 14.25	<b>A prognostic score for nasopharyngeal carcinoma with bone metastasis: development and validation from multicenter</b> Yun Fei Xia (Sun Yat Sen University, Guangzhou, China)	OP-19
14.25 - 16.05	<b>PLENARY 7: Treatment failure and new treatment options in NPC</b> Chair Person: Prof. I. Bing Tan, MD, PhD (Netherlands Cancer Institute/AVL Hospital Amsterdam, NL-Universitas Gadjah Mada Yogyakarta Indonesia)	
14.25 - 14.45	<b>Salvage surgery for local recurrent nasopharyngeal carcinoma</b> Chen Ming Yuan, PhD (Affiliated Hospital of Zunyi Medical College, Guangzhou, China)	PL-17
14.45 - 15.05	<b>Global pattern of nasopharyngeal cancer: correlation of outcome with access to radiotherapy</b> Professor Anna Lee (Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hongkong)	PL-18
15.05 - 16.05	<b>East-West Discussion on NPC Management</b> Chair Person: Prof. Brian O'Sullivan, MB Bch BAO, FRCPC (University of Toronto, Toronto, Canada) and Prof. I. Bing Tan MD, PhD. (Netherlands Cancer Institute-Universitas Gadjah Mada Yogyakarta, Indonesia) a. Kartika Widayati, MD (Universitas Gadjah Mada/Dr. Sardjito Hospital Yogyakarta, Indonesia) b. Prof. Dr. dr. Soehartati G., Sp.Rad(K), Onk.Rad (Universitas Indonesia/Rumah Sakit Cipto Mangunkusumo, Jakarta, Indonesia) c. Farhat, MD (Universitas Sumatera Utara, Medan, Indonesia)	
16.05 - 16.20	Afternoon coffee	
16.20 - 18.00	Break	
18.00 - 21.00	Cultural Night	



Day III. 6 June 2015

**Novel Approaches for NPC Diagnosis and Treatment**

TIME	TOPICS	ABSTRACT NUMBER
	<b>Clinical diagnostics and management (continued)</b>	
08.00 - 08.10	<b>International phase II randomized study on the addition of docetaxel to the combination of cisplatin and 5-fluorouracil in the induction treatment for nasopharyngeal carcinoma in children and adolescents</b> Prof. Enis Ozyar (Departments of Radiation Oncology of Acibadem University, Ankara, Turkey)	OP-20
08.10 - 08.20	<b>Photodynamic therapy in the treatment of nasopharyngeal carcinoma; 12 years of experience in a non-endemic region</b> Maarten Wildeman, MD, PhD (Amsterdam Medical Center, The Netherlands)	OP-21
08.20 - 08.30	<b>Prognostic impact of metastatic status in patients with nasopharyngeal carcinoma</b> Susanna Hilda Hutajulu, MD, PhD (Universitas Gadjah Mada/Dr. Sardjito Hospital, Yogyakarta, Indonesia)	OP-22
08.30 - 08.40	<b>Initial experience of individualized clinical target volume delineation based on tumor extension patterns in intensity modulated radiotherapy for nasopharyngeal carcinoma</b> Ying Sun (Sun Yat Sen University, Guangzhou, China)	OP-23
08.40 - 08.50	<b>Kelch Domain Containing 4 (KLHC4) as a Therapeutic Target for Nasopharyngeal Carcinoma</b> Yi Fan Lian (Sun Yat Sen University, Guangzhou, China)	OP-24
08.50 - 09.00	<b>Development of small molecule inhibitors of latent Epstein-Barr Virus Infection for the Treatment of Nasopharyngeal Carcinoma</b> Troy E. Messick (The Wistar Institute, Philadelphia, USA)	OP-25
<b>09.00 - 10.00</b>	<b>PLENARY 8: Novel Biomarker</b> Chair Person: Prof. Qian Tao (School of Biomedical Sciences, The Chinese University of Hong Kong, China)	
09.00 - 09.20	<b>NPC Diagnosis: Host and Viral Markers</b> Prof. Maria Li Lung (Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong)	PL-19
09.20 - 09.40	<b>The predictive and prognostic biomarker for nasopharyngeal carcinoma</b> Prof. Mu-Sheng Zeng, MD, PhD (Cancer Institute, Sun Yat-sen University, China)	PL-20
09.40 - 09.50	<b>Therapeutic Targeting Of Cancer Stem-Like Cells Using A Wnt Modulator, Icg-001, Enhances The Treatment Outcome Of Ebv-Positive Nasopharyngeal Carcinoma</b> Chan King Chi (Hong Kong Baptist University, Hongkong)	OP-26
09.50 - 10.00	<b>Role of micro RNA in NPC Biology</b> Feifei Liu (University of Toronto, Canada)	OP-27
10.00 - 10.30	Coffee break	
10.30 - 10.40	<b>Announcement of NPC Gordon Research Conference 2016</b> Prof. Maria Li Lung (Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong)	

<b>10.40 - 12.00</b>	<b>PLENARY 9: Immunology and Immunotherapy</b> Chair Person: Prof. Denise Doolan (QIMR Berghofer Medical Research Institute, The University of Queensland, Australia)	
10.40-11.00	<b>Effect of HLA and KIR polymorphism on NPC risk</b> Xiaojiang Gao, PhD (Leidos Biomedical Research, Inc. Frederick National Laboratory for Cancer Research (FNLCR) National Cancer Institute, The Netherlands)	PL-21
11.00-11.20	<b>Exploring the association between potentially neutralizing antibodies against EBV infection and nasopharyngeal carcinoma</b> Anna E. Coghill, MD (National Cancer Institute, Bethesda, Maryland, USA )	PL-22
11.20-11.40	<b>Nasopharyngeal carcinoma immunotherapy to therapeutic vaccine</b> Prof. Rajiv Khanna (QIMR Berghofer Medical Research Institute, University of Queensland, Australia)	PL-23
11.40-12.00	<b>Results of cancer immunotherapy clinical trials</b> Toh Han Chong, MD (National Cancer Centre, Singapore)	PL-24
<b>12.00-12.45</b>	<b>Industrial Lunch Symposium: Concurrent Chemoradiation for Head and Neck Cancer</b>	
12.00-12.20	<b>Radiation Therapy for Head and Neck Cancer</b> Prof. Anna Lee (Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hongkong)	
12.20-12.40	<b>Induction Chemotherapy for Head and Neck Cancer</b> Tb. Djumhana D. Atmakusuma, MD, Ph.D (Universitas Indonesia, Rumah Sakit Cipto Mangunkusumo, Jakarta, Indonesia)	
12.45 - 13.30	Lunch break	
13.30 - 15.10	Satellites for free papers *	
15.10 - 15.40	Closing and announcement for next meeting	

**Poster Presentation**  
**Translational Research on NPC**

NAME	ABSTRACT TITLE	ABSTRACT NUMBER
<b>Wan Lun Hsu</b> Genomics Research Center, Academia Sinica, Taipei	Prediction of nasopharyngeal carcinoma risk by Epstein-Barr virus seromarkers and environmental co-factors: the gene-environment interaction study on nasopharyngeal carcinoma in Taiwan	PP-17
<b>Sukri Rahman, MD</b> Universitas Andalas, Padang, Indonesia	Non-viral risk factors for nasopharyngeal carcinoma in West Sumatra, Indonesia	PP-18
<b>Coco Yin</b>	New prototype VIDAS EBV IgA quick: performance on Chinese and Moroccan populations	PP-19
<b>Dewi Syafriyetti Soeis Marzaini, MD, PhD</b> RSCM Jakarta	The Expression of EBV-LMPI and VEGF as Predictors and Plasma EBV-DNA Levels as Early Marker of Distant Metastasis after Therapy in Nasopharyngeal Cancer	PP-20
<b>Fari Daud, MD</b> Maranatha Christian University	Non-viral risk factors of nasopharyngeal carcinoma in RSUD Sumedang, Indonesia	PP-21
<b>Awal Prasetyo, MD</b> Universitas Diponegoro, Semarang	Diagnostic value of IgA [EBNA1+VCA p-18] ELISA to discriminate nasopharyngeal cancer patients from their unaffected family members	PP-22
<b>Dwi Hartati</b> Universitas Gadjah Mada	Characteristics and factors influencing subjects refusal for blood samples retrieval: lesson from NPC case control study in Yogyakarta – Indonesia	PP-23

PP-21

**Non-viral risk factors of nasopharyngeal carcinoma in RSUD Sumedang, Indonesia**

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**Introduction.** Nasopharyngeal carcinoma (NPC) is a disease with a remarkable racial and geographical distribution. In RSUD Sumedang as well as in Indonesia, NPC is the most frequent malignancy of the head and neck with a high mortality rate. Chronic infection by Epstein-Barr Virus (EBV), environmental factors and genetic factors play an important role in the pathogenesis of NPC. EBV genome was found in almost all cases of NPC and encode viral proteins that contribute to the development of malignancy, especially in undifferentiated NPC the association close to 100%. However, no local data available on the role of the genetic susceptibility and environmental factors, such as dietary factors, smoking and solvent exposure in the pathogenesis of nasopharyngeal carcinoma.

**Aim.** To describe the role of non-viral risk factors on NPC patients in RSUD Sumedang.

**Methods.** The methods used in this research is a survey research design which used a questionnaire. The subjects were all the NPC patients in ENT ambulatory clinic RSUD Sumedang in 2014, who have already been diagnosed by histopathological biopsy. Data of NPC patients was recorded and descriptively analyzed.

**Result and discussion.** The risk factors associated with NPC obtained from the subjects were the following: being a first, second or third degree relative of NPC or other type of cancer, consumption of salted fish  $\geq 3$  times per month, consumption of preserved meat, consumption of herbal medicine, tobacco smoking, exposure to domestic wood cooking fire, and exposure to occupational solvents.

**Notes :**

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## **Non-Viral Risk Factors of Nasopharyngeal Carcinoma in Sumedang Municipal Hospital, Indonesia.**

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### **Abstract**

Nasopharyngeal carcinoma is a disease with a remarkable racial and geographical distribution. In Sumedang Municipal Hospital as well as in Indonesia, nasopharyngeal carcinoma is the first malignancy of the head and neck with a high mortality rate. Chronic infection by Epstein-Barr Virus (EBV), environmental factors and genetic factors play an important role in the pathogenesis of nasopharyngeal carcinoma. EBV genome was found in almost all cases of nasopharyngeal carcinoma and encode viral proteins that contribute to the development of malignancy, especially in undifferentiated nasopharyngeal carcinoma the association close to 100%, but no data about the role of the genetic susceptibility and environmental factors, such as dietary factors, smoking and solvent exposure in the pathogenesis of nasopharyngeal carcinoma. The aim of this study is to describe the frequency of genetic susceptibility and environmental non-viral factors in nasopharyngeal cancer patients in Sumedang Municipal Hospital. This research design was an observational descriptive study using a questionnaire to all patients with nasopharyngeal carcinoma at Sumedang Municipal Hospital in 2014. The subjects were all the nasopharyngeal carcinoma patients in Ear, Nose and Throat polyclinic, which already diagnosed by histopathological biopsy. The results showed that the average age is 45.8 years with the ratio between women : men is 1 : 2.2. The 3 main risk factors in patients with nasopharyngeal carcinoma were, consumption of salted fish more than 3 times per month (75%), smoking more than 10 cigarettes per day (65%) and frequent exposure to wood burning smoke (55%).

Keywords: nasopharyngeal carcinoma, non-viral risk factors

### **Introduction**

Nasopharyngeal cancer is the most common malignancy in the head and neck area and has a unique distribution pattern because several ethnic groups are susceptible to this type of malignancy. According to a report by the International Agency for Research on Cancer, more than 80% of patients with nasopharyngeal cancer are in Asia, especially in East and Southeast Asia. In Indonesia, the prevalence rate of nasopharyngeal cancer is 6.2 / 100,000 people with nearly 13,000 new cases per year and has the highest mortality rate in the world. The incidence of nasopharyngeal cancer

in men is about 2-3 times higher than that of women and is mostly found in productive age with the highest peak at the age of 45-55 years. Therefore, patients with nasopharyngeal cancer will affect economic conditions and become a burden on state health financing<sup>1,2</sup>.

Nasopharyngeal malignant tumors can affect all age levels, but are rarely found under 20 years of age and mostly between 45-54 years. Nasopharyngeal cancer are more common in men than women with the ratio 2-3: 1. Race factor has an important role in NPC. Cantones and Fujian race are the most sufferers of nasopharyngeal cancer, so they are found in South China, Hong Kong, Vietnam, Thailand, Malaysia, Singapore and Indonesia, although some literature reports that it is also found in the Eskimo, Mediterranean and Polinesia race<sup>3</sup>.

The pathogenesis of nasopharyngeal cancer is a multifactorial process due to chronic infection with Epstein-Barr virus (EBV), genetic susceptibility and environmental risk factors. Epstein Barr virus infection is the main cause of nasopharyngeal cancer and the relationship was first identified in 1966 with the discovery of Epstein-Barr virus DNA and EBV nuclear antigen (EBNA) in patients with nasopharyngeal cancer. More than 90% of the world population has been infected with the Epstein-Barr virus, but that does not mean that they will develop nasopharyngeal cancer, there are many other risk factors which can activate EBV that is already present in body cells. These other factors are often referred to as non-viral risk factors for nasopharyngeal cancer. Non-viral risk factors can be in the form of genetic factors, namely if there is a family who also has nasopharyngeal cancer, the habit of consuming salted fish or preserved meat, herbal medicines, exposure to cigarette smoke, exposure to wood burning smoke, exposure to chemicals<sup>4,5</sup>.

The aim of this study is to describe the frequency of genetic susceptibility and environmental non-viral factors in nasopharyngeal cancer patients in Sumedang Municipal Hospital (Rumah Sakit Umum Daerah, Sumedang).

## **Methods**

The research design was an observational descriptive study using a questionnaire given to all patients with nasopharyngeal carcinoma at Sumedang Municipal Hospital in 2014, who have been diagnosed histopathological confirmed as nasopharyngeal

carcinoma. A survey has been conducted using a questionnaire with the following questions:

- being first, second or third degree relative with nasopharyngeal carcinoma or other type of cancers
- consumption of salted fish 1 -  $\geq 3$  times per month
- consumption of preserved meats 1 -  $\geq 3$  times per week
- consumption of herbal-medicine 1 -  $\geq 3$  times per week
- tobacco smoking  $\geq 10$  cigarettes/day
- exposure to domestic wood cooking fires
- exposure to occupational solvents

Descriptive analysis was done with a frequency distribution tabulation.

### Results and Discussion

The results identified 20 patients with nasopharyngeal carcinoma, aged between 27-63 years with a mean age of 45.8 years with the the ratio between women and men is 1 : 2,2. In many studies showed that men are two to three times more likely to develop nasopharyngeal carcinoma than women and the peak age of incidence is between 50 and 60 years<sup>6</sup>.

The results of the questionnaire indicate the risk factors in nasopharyngeal carcinoma patients are as follow:

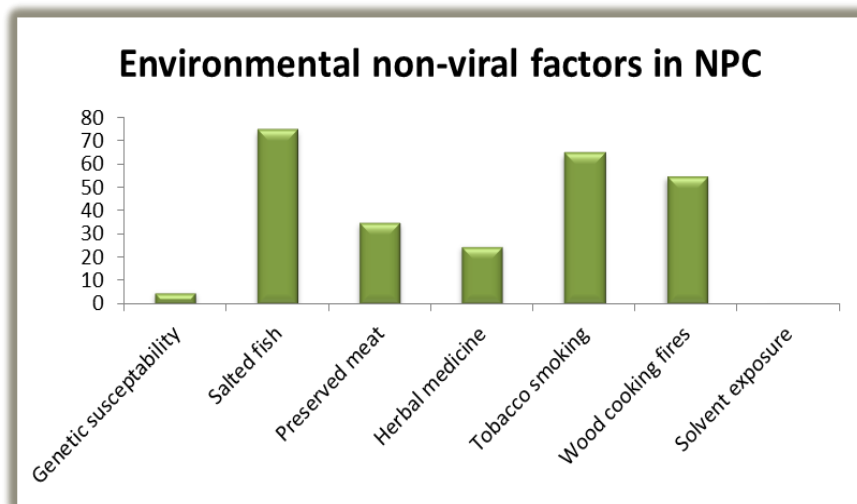


Fig 1. Distribution of non-viral risk factors of nasopharyngeal carcinoma begins with the most frequent: consumption of salted fish (75%), tobacco smoking (65%), exposure to domestic wood cooking fires (55%), consumption of preserved meat (35%), herbal medicine (25%), genetic susceptibility (5%).

This percentage of risk factors in Fig 1 is the total number of patients exposed to the risk factors compared to the total patients and in one patient can get more than one risk factors. The result showed that the three main risk factors in nasopharyngeal carcinoma patients in Sumedang Municipal Hospital were, consumption of salted fish more than 3 times per month (75%), smoking more than 10 cigarettes per day (65%) and frequent exposure to wood burning smoke (55%).

The consumption of salted fish is one of the most frequent reported risk factors for nasopharyngeal cancer, this is due to the carcinogen nitrosamines contained in salted fish. Most nitrosamines are in the form of nitrosodimethylamine compounds which are mainly absorbed in the respiratory tract and digestive tract. The process of malignancy can occur due to the metabolism of nitrosamine which results in DNA mutations. Based on the research, it was found that exposure to nitrosamine between 2.5 - 15  $\mu\text{g} / \text{m}^3$  over a period of 10 years was associated with the incidence of malignancy. Other researchers claim that excessive consumption of salted fish before age 10 is associated with an increased risk of developing nasopharyngeal cancer. In South China, salted fish is the initial food often given by parents to babies and children, increasing the incidence of nasopharyngeal cancer. Salted fish also contains mutagenic bacteria and components that can activate the EBV virus so that it can increase the incidence of nasopharyngeal cancer. Foods that are preserved by means of salting can also increase the risk of nasopharyngeal cancer such as salted vegetables, salted shrimp, salted eggs and other salted foods<sup>4,5</sup>.

In China, the relative risk of nasopharyngeal carcinoma in people who consume salted fish once per week has a 1.4 - 3.2 times higher risk of developing nasopharyngeal carcinoma than those who rarely or never consume salted fish. In people who consume it almost every day the risk varies from 1.8 to 7.5 times. The risk of nasopharyngeal cancer also increases in a group of people who frequently consume preserved foods, including meat, eggs, fruits and vegetables<sup>6</sup>. In this research 35% of the nasopharyngeal carcinoma patients consume preserved meat minimally one time per week.

Cigarette smoke contains around 4000 chemical compounds and more than 60 of these chemical compounds are carcinogens. Several studies reported that in heavy smokers the incidence of nasopharyngeal cancer increased 2-4 times higher than nonsmokers. Active smokers with cigarette consumption of more than 30 packs a year

can increase the incidence of nasopharyngeal carcinoma<sup>5</sup>. The odds ratio for those who smoked for 25 years compared with non-smokers was 1,7 and passive smoking during childhood or adult life was not associated with an increased risk of disease<sup>7</sup>.

The risk of developing nasopharyngeal cancer increases if we are often exposed to smoke from burning wood or wood dust that has accumulated for a long time. Wood dust causes irritation and inflammation of the nasopharyngeal epithelium. The nasal cavity is the main entry point for gases or smoke into the human body. The nasopharynx is the main area for trapping of particles to facilitate absorption of chemicals into the nasopharyngeal epithelium and these inhaled substances are carcinogens. Exposure to wood smoke resulting from burning firewood for cooking for more than 10 years can increase the incidence of nasopharyngeal cancer by about 6 times<sup>4,5</sup>.

Herbal medicine as the risk factor of nasopharyngeal carcinoma has been reported by several studies. There is an association between the use of herbal medicines with the risk of developing nasopharynx carcinoma. In one case control study conducted in the Philippines noted that the use of herbal medicines can increase the risk of nasopharyngeal carcinoma by 2.5 times. However, other researchers said that slow-cooked herbal medicines and Cantonese-style herbal teas were associated with a reduced risk of nasopharyngeal carcinoma, it means there is still uncertainty<sup>6</sup>. In this research the used of herbal medicine is 25%.

Family history with nasopharyngeal carcinoma or other cancers is thought to be related to nasopharyngeal carcinoma risk. Several studies have shown that the risk of nasopharyngeal carcinoma is significant higher in first degree relatives than in the general population. It means that genetic factors contribute to the development of nasopharyngeal carcinoma. Research showed that this genetic risk factor is due to the polymorphism of several metabolic enzyme genes such as CYP2E1 and GSTM1 and some DNA repair genes such as XRCC1 and hOGG1 and certain HLA genes<sup>8</sup>. In this study, only 5% with genetic susceptibility, this can be due to ignorance of the existence of cancer in the family.

Apart from avoiding the risk factors that have been mentioned above, the consumption of tea and fresh fruits can reduce the incidence of nasopharyngeal cancer because they contain antioxidants that can change the chemical structure of



nitrosamines. Fresh fruit and vegetables also contain lots of vitamin C so that it can inhibit the formation of nitrosamines and prevent mutagenesis and carcinogenesis.

## Conclusion

The findings of this study showed that the average age of the nasopharyngeal carcinoma is 45.8 years with the ratio women to men is 1 : 2.2. The main risk factors (with percentage more than 50%) in nasopharyngeal carcinoma patients in Sumedang Municipal Hospital in 2014 were, consumption of salted fish more than 3 times per month (75%), smoking more than 10 cigarettes per day (65%) and frequent exposure to wood burning smoke (55%). This study had a limitation, because of the small number of the patients.

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