

# Nasopharyngeal Carcinoma Database

**K C Pua\***, **A S B Khoo\*\***, **Y Y Yap\*\*\***, **S K Subramaniam\*\*\*\***, **C A Ong\*\*\*\*\***, **G Gopala Krishnan\*\*\*\*\***, **H Shahid\*\*\*\*\***, **The Malaysian Nasopharyngeal Carcinoma Study Group#**

\*Department of Otorhinolaryngology, Hospital Pulau Pinang, Jalan Residensi, 10990 Penang, \*\*Molecular Pathology Unit, Cancer Research Centre, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, \*\*\*Department of Surgery, Clinical Campus Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur, \*\*\*\*Department of Otorhinolaryngology, Head and Neck Surgery, Sarawak General Hospital, Jalan Hospital, 53586 Kuching, Sarawak, \*\*\*\*\*ENT Department, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, \*\*\*\*\*Department of Otorhinolaryngology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, \*\*\*\*\* Department of ORL-Head and Neck Surgery, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

## SUMMARY

**Nasopharyngeal carcinoma (NPC) is a cancer which is common in Asia. We report the establishment and early results of a multi-institutional prospective study of nasopharyngeal carcinoma, which seeks to systematically collect data as well as blood and tumour tissue samples from patients diagnosed with nasopharyngeal cancer at six centres in Malaysia. A total of 484 confirmed NPC cases were reported from the six participating centres between 1st July 2007 and 29th February 2008. Of these, 225 were newly diagnosed cases, 53 were recurrent cases and 206 were in remission at the time of reporting. Amongst the newly diagnosed cases, the most common presenting symptom was the presence of neck lumps (42%). Ophthalmic-neurologic symptoms were the presenting symptoms of 11% of the new cases. The majority of cases (75%) presented at stage III/IV.**

## KEY WORDS:

*Nasopharyngeal carcinoma, Database, Symptom, Diagnosis, Multi-center*

## INTRODUCTION

Although Nasopharyngeal Carcinoma (NPC) is rare in most populations, it is a leading form of cancer in a few well-defined populations, including natives of southern China, Southeast Asia, the Arctic, and the Middle East/North Africa. The distinctive racial/ethnic and geographic distribution of NPC worldwide suggests that both environmental factors and genetic traits contribute to its development.

Nasopharyngeal carcinoma (NPC) is a prevalent cancer in Malaysia. According to the National Cancer Registry, there were 1,125 incident cases of NPC in Peninsular Malaysia in 2003, where it was the second most common cancer among males<sup>1</sup>. The age-standardized incidence was 10.2 and 3.6 per 100,000 of the population for males and females, respectively, in Peninsular Malaysia<sup>1</sup>. The incidence is particularly high in some native groups in Sarawak<sup>2</sup>.

While there have been several hospital studies on NPC in Malaysia<sup>3,4,5,6</sup>, there is a lack of multi-centre studies on the disease. In addition, there is a paucity of information of the clinical outcome of NPC patients in Malaysia. In order to

collect and analyse the pattern of presentation and clinical outcome of NPC patients in Malaysia and to collect samples for research, we have established a multi-institutional study of NPC in Malaysia. The linkage of high quality clinical information to the bio-specimens will open up new avenues of research that could help prevent, treat and control this disease.

The study involves six major tertiary referral centres representing parts of Peninsular Malaysia (one centre each in Penang and Kelantan and two centres in Kuala Lumpur) and East Malaysia (one centre each in Sabah and Sarawak).

In this preliminary report, we present the demographic and clinical information of the patients in the first eight months of the establishment of the Malaysian NPC Clinical Outcome database.

## MATERIALS AND METHODS

### Centres

The NPC clinical outcome study is a multi-centre, prospective study which recruited all patients with confirmed NPC regardless of the stage, histopathology and duration of disease, who were seen at the participating sites: Penang Hospital, Kuala Lumpur Hospital/Universiti Putra Malaysia (UPM), Sarawak General Hospital (Hospital Umum Sarawak)/Universiti Malaysia Sarawak (UNIMAS), Queen Elizabeth Hospital, Sabah, University of Malaya Medical Centre (UMMC) and Universiti Sains Malaysia (USM) Hospital, Kubang Kerian, Kelantan. The study was monitored and data was managed by the Department of Otorhinolaryngology and the Clinical Research Centre, Penang Hospital in compliance with patient data protection. This study is approved by the Medical Research and Ethics Committee of the Ministry of Health Malaysia and the institutional ethics committees of UMMC and the USM Hospital.

### Inclusion criteria and data collection

All cases reported between 1st July 2007 and 29th February 2008, were included in this preliminary analysis. We established a secure clinical database (<https://app.acrm.org.my/npc/>) to enable secure real-time collection of data. All centres were responsible for entering

data through a web-based interface into the database. All confirmed cases of nasopharyngeal cancer patients were recruited to the study and clinical data was collected by a research assistant or doctor responsible for the care of the patient. The histopathology was classified according to the World Health Organization Classification of Nasopharyngeal Carcinoma (WHO I, WHO II and WHO III)<sup>7</sup>. The disease was staged according to the AJCC Staging for Nasopharyngeal Carcinoma 2002<sup>8</sup>.

The data was cleaned by the database manager and reviewed. The cases were analysed separately for newly diagnosed cases (New), recurrent cases (Recurrent), and cases which were already in remission at the time of diagnosis (Remission).

## RESULTS

### *Cases reported by Centres (Table I)*

Between July 2007 and February 2008, a total of 484 confirmed NPC cases were reported from the six participating centres. Of these, 225 were newly diagnosed cases, 53 were recurrent cases and 206 were in remission at the time of reporting.

### *Socio-demographic Distribution of Cases (Table II and III)*

As has been described previously in other populations<sup>9,10</sup>, we found a higher incidence of NPC in men compared to women: the male: female ratio was ~3:1 for both newly diagnosed and recurrent cases. Seventy-one percent of the new cases were in the productive working age group of 21 to 60 years. Among the new cases, 49% were Chinese, 22% Malays, 1% Indians and 28% were of other ethnic groups (primarily, the natives of Sabah and Sarawak). The majority were non-professionals (96%) without tertiary education

(98%). This reflects the group of patients commonly treated in public hospitals throughout the country.

### *First Presenting symptoms, histopathology types & Staging (Table IV)*

The most common presenting symptom was neck lumps (42%), followed by nasal symptoms (30%). Notably, 11% of the new patients had ophthalmo-neurologic symptoms i.e. headache and cranial nerves palsy. Ninety-seven percent of the new cases were non-keratinising carcinomas (WHO type II and III). Seventy-five percent of the newly diagnosed patients presented at late stages (Stages III/IV).

## DISCUSSION AND CONCLUSION

Our preliminary findings show that the spectrum of first presenting symptoms from our cases were similar to those reported elsewhere (Table V)<sup>6,9,10</sup>, in which neck lumps were the most common presentation and about a tenth of cases presented with ophthalmo-neurologic symptoms. Despite advances in diagnosis of NPC, the percentage of cases presenting at late stages remains high (Table VI)<sup>6</sup>.

Since the database became operational only eight months ago it is still too early to analyse treatment and clinical outcome. Collectively, the fact that nearly 80% of patients present at late stages as evidenced by our data suggests that the development and effective implementation of screening methods could help in early detection of NPC thereby improving the survival outcome of NPC patients in Malaysia. Further work is on-going to recruit more patients and to collect patient data during subsequent follow up visits. This might throw more light on survival outcome and prognostic factors.

**Table I: Total NPC cases reported from six selected centers in Malaysia**

Centre	New	Recurrent	Remission	Total
Hospital Pulau Pinang	90	33	45	168
Hospital Kuala Lumpur / UPM	52	16	54	122
Kuching General Hospital / UNIMAS	11	0	62	73
Queen Elizabeth Hospital, Sabah	62	1	0	63
University of Malaya Medical Centre (UMMC)	7	3	44	54
Hospital USM, Kubang Kerian	3	0	1	4
<b>Total</b>	<b>225</b>	<b>53</b>	<b>206</b>	<b>484</b>

**Table II: Age and Sex Distribution of Patients Reported with Nasopharyngeal Carcinoma**

Cases	New N (%)		Recurrent N (%)		Remission N (%)	
<b>Gender</b>						
Male	173	(77)	40	(75)	138	(67)
Female	52	(23)	13	(25)	68	(33)
<b>Age distribution</b>						
11-20 yrs	5	(2)	1	(2)	4	(2)
21-30 yrs	19	(8)	2	(4)	7	(3)
31-40 yrs	23	(10)	7	(13)	33	(16)
41-50 yrs	57	(25)	5	(9)	43	(21)
51-60 yrs	61	(28)	23	(43)	62	(30)
61-70 yrs	46	(20)	13	(25)	45	(22)
71-80 yrs	14	(7)	2	(4)	11	(5)
81-90 yrs	0	(0)	0	(0)	1	(1)

**Table III: Ethnicity, Education Status, Occupation and Social Risk Factors of Patients Reported with Nasopharyngeal Carcinoma**

Cases	New N (%)		Recurrent N (%)		Remission N (%)	
<b>Ethnicity</b>						
Malay	50	(22)	4	(7)	49	(24)
Chinese	110	(49)	48	(89)	122	(60)
Indians	3	(1)	0	(0)	2	(1)
Others	62	(28)	1	(4)	33	(15)
<b>Education</b>						
Primary	82	(38)	16	(32)	66	(35)
Secondary	96	(43)	25	(50)	79	(42)
Tertiary	5	(2)	2	(4)	14	(7)
No formal education	38	(17)	7	(14)	30	(16)
<b>Occupation</b>						
Service	57	(25)	13	(25)	48	(23)
Labourer	30	(13)	7	(13)	15	(8)
Unemployed	52	(23)	21	(40)	90	(44)
Agriculture	12	(5)	0	(0)	4	(2)
Professional	8	(4)	1	(2)	6	(3)
Others	66	(30)	11	(20)	42	(20)
<b>Social Risk Factors</b>						
Tobacco consumption	124	(55)	23	(43)	72	(35)
Alcohol consumption	83	(37)	13	(25)	43	(21)

**Table IV: First presenting symptoms, Histological types and Stage at Initial diagnosis of patients**

Cases	New N (%)		Recurrent N (%)		Remission N (%)	
<b>First Presenting Symptoms</b>						
Neck lumps	95	(42)	16	(31)	82	(40)
Nasal obstruction	67	(30)	15	(27)	72	(35)
Ear	25	(11)	5	(10)	23	(11)
Headache	11	(5)	3	(6)	5	(2)
Cranial nerve	13	(6)	7	(13)	8	(4)
Others	14	(6)	7	(13)	16	(8)
<b>Histological Types</b>						
WHO Type I	6	(3)	4	(8)	4	(2)
WHO Type II/III	211	(97)	44	(92)	180	(98)
<b>Staging at initial diagnosis*</b>						
Stage I	7	(4)	2	(5)	6	(4)
Stage II	35	(21)	10	(27)	37	(27)
Stage III	47	(28)	13	(34)	52	(38)
Stage IV	78	(47)	13	(34)	43	(31)

\* The stage at presentation when diagnosed to have NPC for the first time, prior to the appearance of the recurrence (if applicable)

**Table V: Comparison of First Presenting Symptoms of NPC**

Symptoms	NPC Database Malaysia 2007/2008 N (%)	University Hospital, Kuala Lumpur (6) 1994/1997 N (%)	North American Series (9) N (%)	Prince of Wales Hospital, Hong Kong (10) 1991 N (%)
Neck Mass	95 (42)	50(50)	54(36)	188(43)
Nasal	67(30)	26(26)	32(21)	131(30)
Ear	25(11)	12(12)	44(29)	75(17)
Ophthalmo-neurologic	24(11)	11(11)	12(8)	39(9)
Others	14(6)	1(1)	9(6)	4(1)
Total	225(100)	100(100)	151(100)	437(100)

**Table VI: Comparison of Stage of Disease at Diagnosis of NPC**

Staging	NPC Database 2007/2008 (%)	University Hospital, Kuala Lumpur (6) 1994/1997 (%)
Stage I	7(4)	3(3)
Stage II	35(21)	3(3)
Stage III	47(28)	14(14)
Stage IV	78(47)	80(80)
Total	167(100)	100(100)

# Note: NPC Database used AJCC Staging (2002) while University Hospital series used UICC Staging 1987

## ACKNOWLEDGEMENT

The authors would like to sincerely thank the Director General of Health, Malaysia for his permission to publish this paper. We wish to thank the Director of the Institute for Medical Research, the Director of the Network of Clinical Research Centres as well as the Directors of the participating centres for their support. We wish to acknowledge the contributions by otorhinolaryngologists, oncologists, radiotherapists, and pathologists of the participating centres as well as the staff of the Clinical Research Centres of Kuala Lumpur Hospital and Penang Hospital as well as the Cancer Research Initiatives Foundation and the Institute for Medical Research for their contribution and support. This project was funded by the Ministry of Health, Malaysia (Project code: JPP-IMR 06-060).

## Note:

### #Malaysian Nasopharyngeal Carcinoma Study Group

- Hospital Pulau Pinang: K C Pua (Project Leader), S Subathra, Y S Ee, M Goh, A H Rahmah, C H Fong, N Punithavathi, L M Ong
- Hospital Kuala Lumpur/UPM: Y Y Yap, B D Dipak, R Deepak, F N Lau, P Shalini, M A Atiliyana
- University of Malaya: G Gopala Krishnan, S Shamshinder, M Anura, A Z Bustam, M Saad, M Dahalil, L M Looi, P Shahfinaz, O Hashim, C C Ng, O Rahmat, J Amin
- Institute for Medical Research: A S B Khoo, (Programme Leader), N M Kumaran
- Cancer Research Initiatives Foundation: S H Teo, L F Yap
- Sarawak General Hospital/UNIMAS: S K Subramaniam, T S Tiong, U H Sim, T W Tharumalingam, D Norlida, M Zulkarnaen, W H Lai
- Queen Elizabeth Hospital: C A Ong, S Bokari, C L Lum, A Vivekananda, A Othman, D Jayendran, A Kam
- Hospital USM Kubang Kerian: S Hassan, B Biswal, H Nik Fariza, H A Mubassir, A H Suzina Sheikh

### For further enquiries regarding the NPC Database, please contact:

Manager

Nasopharyngeal Carcinoma Treatment Outcome Database

Clinical Research Centre

Penang General Hospital

Residensi Road

10990 Penang, Malaysia

Tel: 604- 228 9246/ 227 4982

Fax: 604- 226 1579

Email: npc@acrm.org.my

Website: <https://app.acrm.org.my/NPC>

## REFERENCES

1. Lim GCC, Halimah YY (Eds). Second Report of the National Cancer Registry. Cancer Incidence in Malaysia 2003. National Cancer Registry. Kuala Lumpur 2004.
2. Devi BCR, Pisani P, Tang TS, Parkin DM. High incidence of nasopharyngeal carcinoma in native people of Sarawak, Borneo Island. *Cancer Epi Bio Prev* 2004; 13: 482-85.
3. Tiong TS, Selva KS. Clinical Presentation of NPC in Sarawak, Malaysia. *Med J Malaysia* 2005; 60: 624-28.
4. Indudharan R, Valuyeetham KA, Kankan T, Sidek DS 1997, Nasopharyngeal carcinoma: clinical trends. *J Laryngol Otol* 1997; 111: 724-29.
5. Suzina SA, Hamzah M. Clinical presentation of patients with nasopharyngeal carcinoma. *Med J Malaysia* 2003; 58: 539-45.
6. Prasad U, Pua KC. Nasopharyngeal Carcinoma: A Delay in Diagnosis *Med J Malaysia* 2000; 55: 230-35.
7. Shanmugaratnam K (1978) Histological Typing of Upper Respiratory Tract Tumours. International Histological Typing of Tumours No. 19 World Health Organization, 1978: 19-21.
8. Greene FL, Page DL, Fleming ID, Fritz A, Balch CM, Haller DG, Morrow M (eds). *AJCC Cancer Staging Manual* (6th. Edition) Chicago: Springer 2002.
9. Neel III HB, Taylor WF. Clinical presentation and diagnosis of nasopharyngeal carcinoma: Current Status presented at International Symposium on Nasopharyngeal Carcinoma, Kuala Lumpur, 1982.
10. Skinne DW, van Hasselt CA, Tsao SY. Nasopharyngeal carcinoma: a study of the modes of presentation. *Annals of Otolaryngology and Rhinology* 1991; 100: 544.